AN ABSTRACT OF THE DISSERTATION OF

Khomson Suttisintong for the degree of Doctor of Philosophy in Chemistry

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Title: Studies Toward the Total Synthesis of Sanglifehrin A.

Abstract approved:_____

James D. White

Studies toward synthesis of subunits of sanglifehrin A, an immunosuppressant featuring a highly substituted [5,5]-spirolactam moiety as well as a 22-membered macrocycle are described. The macrolactone contains a peptidic backbone characterized by an unusual *β*–substituted *(S)*-piperazic acid and *(S)-m*-hydroxyphenylalanine units. These studies resulted in the synthesis of advanced intermediate **358** which contains all of the carbon atoms of the C1-C25 macrolactone of sanglifehrin A, and **251** which bears the C31-C41 carbon skeleton of the [5,5]-spirolactam moiety of sanglifehrin A. A Masamune anti-aldol reaction of aldehyde **294** and ester **285** furnished alcohol **295** in a second generation approach to carboxylic acid **242**, while a third generation route toward **242** improved the yield and required fewer synthetic steps. An asymmetric, catalytic phase-transfer method was used to introduce an α-amino function into **331** in the synthesis of *(S)-m*-hydroxyphenylalanine derivative **244**. Assembly of **244**, piperazic acid **113** and L-valine derivative **336** into tripeptide **241** using a racemization-free peptide coupling

method is described. The synthesis of C31-C37 aldehyde **253** exploited double asymmetric crotylation to set in place the correct configuration of alternating hydroxyl and methyl groups at C33, 34, 35 and 36.

Studies Toward the Total Synthesis of Sanglifehrin A

by

Khomson Suttisintong

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APPROVED:

Major Professor, representing Chemistry

Chair of the Department of Chemistry

Dean of the Graduate School

I understand that my dissertation will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my dissertation to any reader upon request.

Khomson Suttisintong, Author

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TABLE OF CONTENTS

Page

TABLE OF CONTENTS (Continued)

Page

TABLE OF CONTENTS (Continued)

Page

LIST OF FIGURES

LIST OF TABLES

Dedicated with love to

my parents

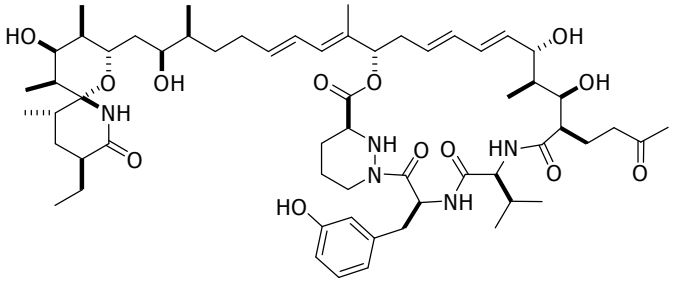
CHAPTER 1: INTRODUCTION

1.1 General Introduction

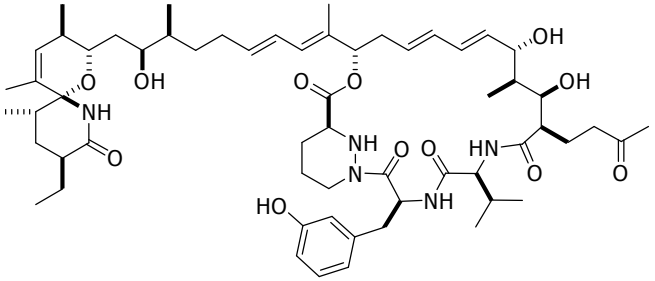
The sanglifehrins (Figure 1.1), a novel class of macrolides, were initially discovered in a soil sample from Dembo-Bridge in Malawi by scientists at Novartis[1] in 1997. Produced by *Streptomyces* sp A92-308110, sanglifehrins, especially sanglifehrin A (SFA, **1**), possess impressive biological properties.[2, 3] These include strong binding to cyclophilin A (CypA) which leads to inhibition of both B-cell and T-cell proliferation.

The structures of sanglifehrins A-D have been fully elucidated by spectroscopic and X-ray crystallographic techniques[4] and are shown in Figure 1.1. Key features of sanglifehrins include a novel, highly substituted [5,5]spirolactam moiety and a 22-membered macrocycle containing a peptidic backbone characterized by an unusual *β*–substituted *(S)*-piperazic acid and a *(S)*-*m*-hydroxyphenylalanine unit.

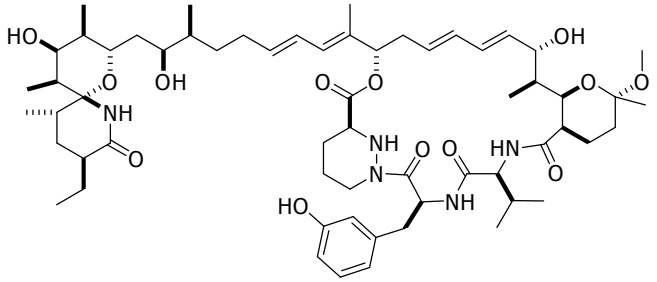
Sanglifehrin A (SFA, **1**) is the most abundant natural product from this microbial strain and has the highest affinity for cyclophilins A, B and C. Its capacity for inhibiting mitogen-induced B-cell proliferation without influencing T-cell receptor-mediated cytokine production is also notable.[5] The striking properties of SFA have attracted the interest of many research groups. Thus, the first synthesis was achieved by Nicolaou[6] and coworkers in 1999 and a second synthesis was completed by the Paquette[7] research team in 2002.



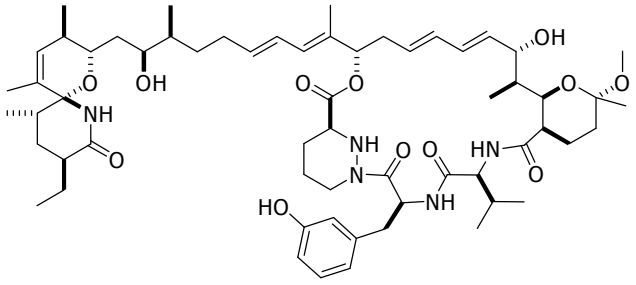
Sanglifehrin A (**1**)



Sanglifehrin B (**2**)



Sanglifehrin C (**3**)



Sanglifehrin D (**4**)

Figure 1.1 Sanglifehrins A-D

1.2 Isolation and Structural Assignment to Sanglifehrins

The sanglifehrins were found during screening of actinomycete strains with a cyclophilin-binding assay.[2] They were isolated and purified by extraction and several chromatographic, activity-guided steps. The chemical structure and absolute configuration of sanglifehrins A, B, C, and D were determined unambiguously by NMR techniques and by X-ray crystallography of the complex formed with cyclophilin A.[4] Sanglifegrins A and B are true natural products according to analytical HPLC survey during the fermentation process, whereas sanglifehrins C and D are artifacts formed from sanglifehrin A and B, respectively, during isolation in the presence of methanol.

The molecular formulas of the sanglifehrins were established by FAB-MS and elemental analysis to be $C_{60}H_{91}N_5O_{13}$ (*m/z* 1096, $[M+Li]^+$) for sanglifehrin A, $C_{60}H_{89}N_5O_{12}$ (*m/z* 1078, $[M+Li]^+$) for B, $C_{61}H_{93}N_5O_{13}$ (*m/z* 1110, $[M+Li]^+$) for C, and $C_{61}H_{91}N_5O_{12}$ (*m/z* 1092, $[M+Li]^+$) for D. The UV and IR spectra of the four compounds resembled each other, suggesting their structural similarity. The characteristic, strong absorption band in the IR spectra of sanglifehrins at 1645 – 1650 cm^{-1} indicated the presence of several amide linkages. NMR data collected by Fehr and co-workers revealed that the sanglifehrins were constituted of three main segments, specifically a 22 membered macrolide (C1-C23), a linker subunit (C24-C32), and a unique spirolactam system (C33-N42) (Figure 1.2).

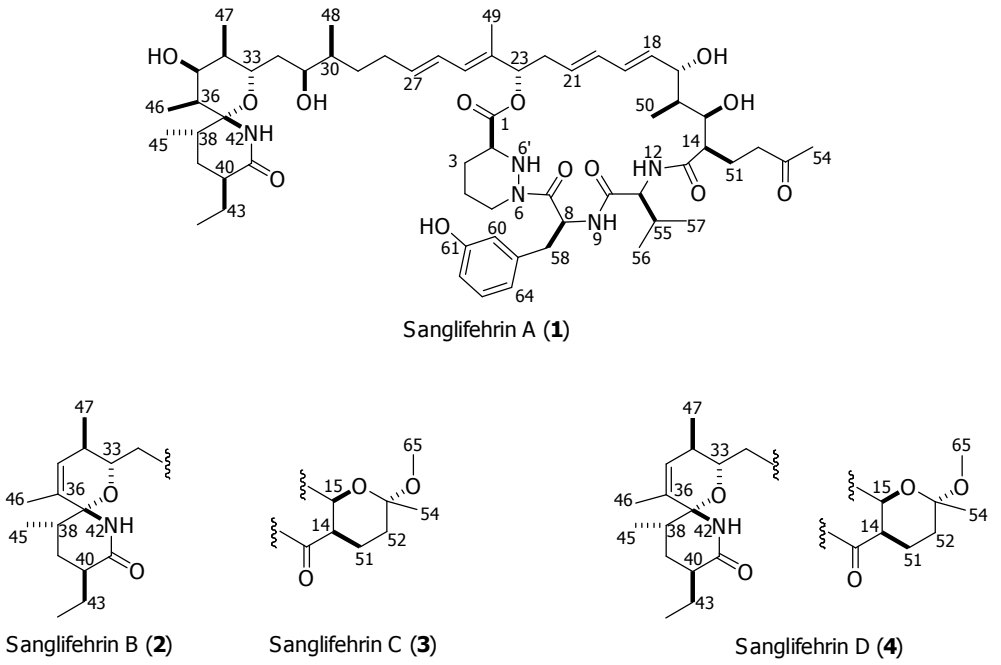


Figure 1.2 Carbon numbering of sanglifehrins A-D

A tripeptide embedded in the macrolide consisting of valine, *m*-tyrosine, and 1,2-piperazine-3-carboxylic acid was recognized using sequential NOE's. An inverse ^{1}H-^{15}N-HSQC experiment confirmed the presence of the hydrazide group of the 1,2-piperazine-3-carboxylic acid moiety from the ^{15}N shift of NH-6′ to high field (83 ppm); all other NH's have typical amide chemical shifts in the range 115-130 ppm. The disappearance of the C15-OH proton and an upfield shift of C53 from 208.1 to 98.6 ppm, along with the presence of methoxy methyl protons at C65, established that cyclic ketal formation had occurred in sanglifehrins C and D.

The C24-C32 linker connecting the macrolide with the spirolactam system was shown to contain a methyl-substituted conjugated (*E*,*E*)-diene and an aliphatic portion

(C28-C32) which bears vicinal methyl and hydroxyl substituents (C30 and C31, respectively). This linker unit appears in all four sanglifehrins.

The spirolactam subunit was shown to consist of two 6-membered rings fused at C37; this carbon signal appeared at 86.9 ppm in the ^{13}C-NMR spectrum of sanglifehrin A. One of these spiro fused rings is a tetrahydropyran and the other is a δ-lactam. Sanglifehrins A and C have the tetrahydropyran ring of the spirolactam in a chair conformation with two equatorial methyl groups and an axial OH group, whereas the corresponding ring in sanglifehrins B and D possesses a C35-C36 double bond which probably arises from dehydration of the C35 hydroxyl of sanglifehrins A and C, respectively. It was shown that the lactam ring in SFA is in a boat conformation presumably to allow the methyl group at C38 and the ethyl group at C40 to assume an equatorial orientation.

The absolute configuration of sanglifehrin A was confirmed by an X-ray crystallographic analysis of the cyclophilin A/sanglifehrin A complex at 1.6 Å resolution. The absolute configurations of sanglifehrins B, C, and D were deduced by spectroscopic and chemical correlation with sanglifehrin A.

1.3 Biological Activity of the Sanglifehrins

Sanglifehrins A and B were shown to bind very tightly to cyclophilin A (CyPA). Their affinities were approximately twenty times higher than that of cyclosporine A (CsA).[2] Sanglifehrin A showed the strongest binding to cyclophilins

A, B and C, with an IC_{50} of 0.05-0.09 for all three cyclophilins (Table 1.1). Sanglifehrins C and D containing a cyclic acetal showed a more than 10-fold decrease in binding to CypA and possessed an affinity in the same range as that of CsA.

Table 1.1 Relative IC_{50} values of sanglifehrins for binding to cyclophilins A, B and C

Compound	CYP-A	CYP-B	CYP-C
Sanglifehrin A	0.05±0.02	0.09±0.02	0.07±0.03
Sanglifehrin B	0.05±0.01	0.56±0.23	0.12±0.03
Sanglifehrin C	0.61±0.19	2.69±0.74	0.33±0.01
Sanglifehrin D	0.71±0.14	2.63±0.62	0.62±0.03

The immunosuppressive activities of sanglifehrins A, B, C and D were assessed in two-way MLR (Mixed Lymphocyte Reaction) experiments. The results are shown in Table 1.2. Sanglifehrins A and B showed IC_{50} values of 170 nM and 102 nM, respectively. Although both compounds showed affinity for cyclophilin A at a level 20-fold higher than that of CsA, their immunosuppressive activity in the MLR experiment was approximately 10-fold lower.

Table 1.2 Activity of sanglifehrins A, B, C and D and cyclosporine A in the murine mixed-lymphocyte reaction.

Compound	Mean IC_{50} [nM][a]	Relative IC_{50}[b]
Sanglifehrin A	170 ± 15	16
Sanglifehrin B	102 ± 7	10
Sanglifehrin C	1200 ± 104	113
Sanglifehrin D	630 ± 87	60
Cyclosporin A	10.6 ± 0.8	1

[a] Results are expressed as a mean ± SEM of IC_{50} values in nM; results of 3~4 independent experiments. (SEM = Standard Error of Mean)

[b] Ratio of the IC_{50} values of sanglifehrin and cyclosporine A

1.4 References

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CHAPTER 2: PREVIOUS SYNTHETIC STUDIES OF SANGLIFEHRIN A

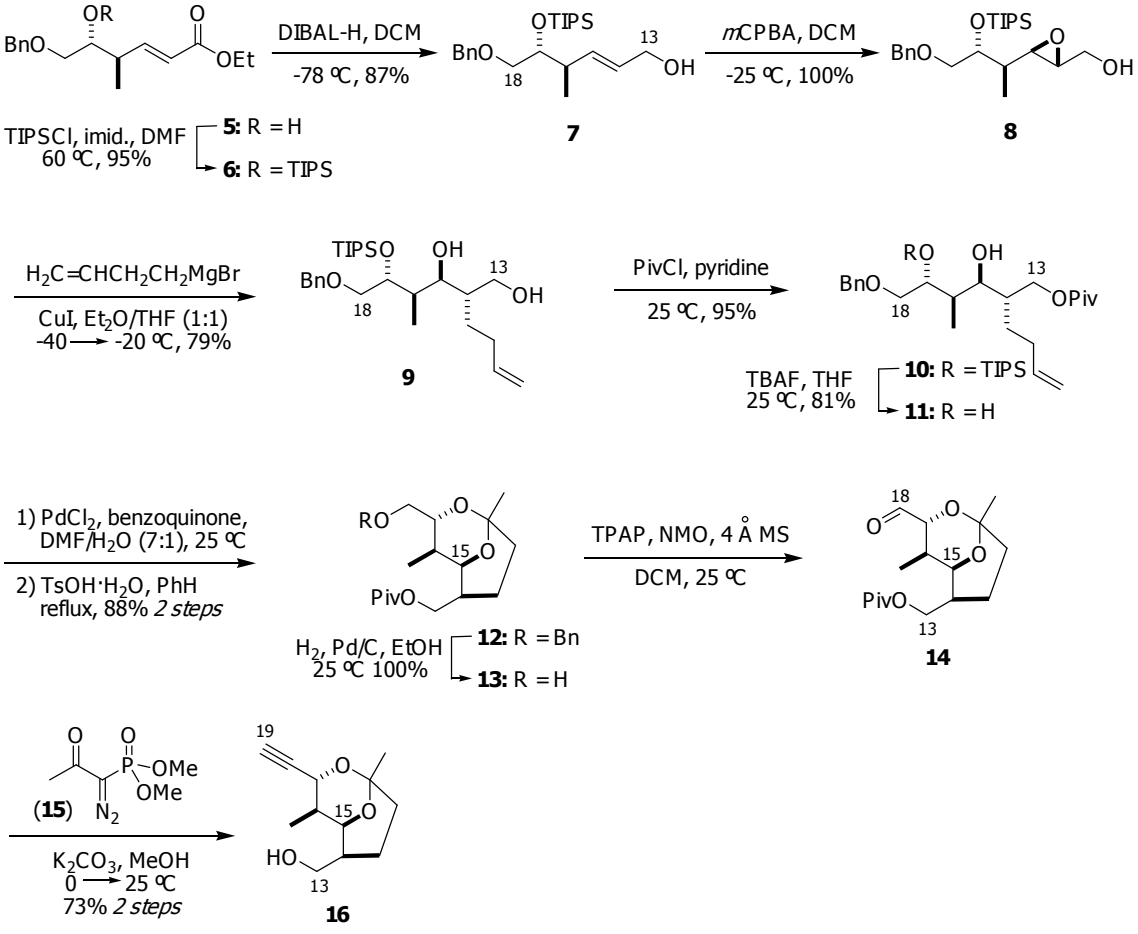
There have been two completed syntheses of sanglifehrin A to date. The first total synthesis was reported in 2000 by Nicolaou and coworkers, about three years after its isolation.[1] The second synthesis was published in 2002 by the Paquette research group.[2] Many syntheses of fragments of sanglifehrin A have also been reported.[3-11]

2.1 Nicolaou's Total Synthesis of Sanglifehrin A (2000)

2.1.1 Synthesis of the C13-C19 Acetylenic Ketal Portion

Nicolaou's route to sanglifehrin A commenced with the synthesis of aldehyde **14** as shown in Scheme 2.1. The known α,β-unsaturated ester **5**[12] was converted to triisopropylsilyl ether **6** which was reduced with diisobutylaluminum hydride to give allylic alcohol **7**. Epoxidation of allylic alcohol **7** with *m*-chloroperoxybenzoic acid furnished epoxide **8** in quantitative yield and good selectivity (β:α epoxide ratio ~6:1). Regiospecific ring opening[13] of the epoxide with 3-butenylmagnesium bromide[14] in the presence of copper(I) iodide afforded olefinic diol **9**, which was chemoselectively converted to the primary pivaloate **10**. After removal of the triisopropylsilyl protecting group from **10** with tetra-*n*-butylammonium fluoride to give diol **11**, Wacker oxidation of the terminal alkene followed by acid-induced internal ketalization of the intermediate methyl ketone provided ketal **12** in excellent yield. The benzyl protecting

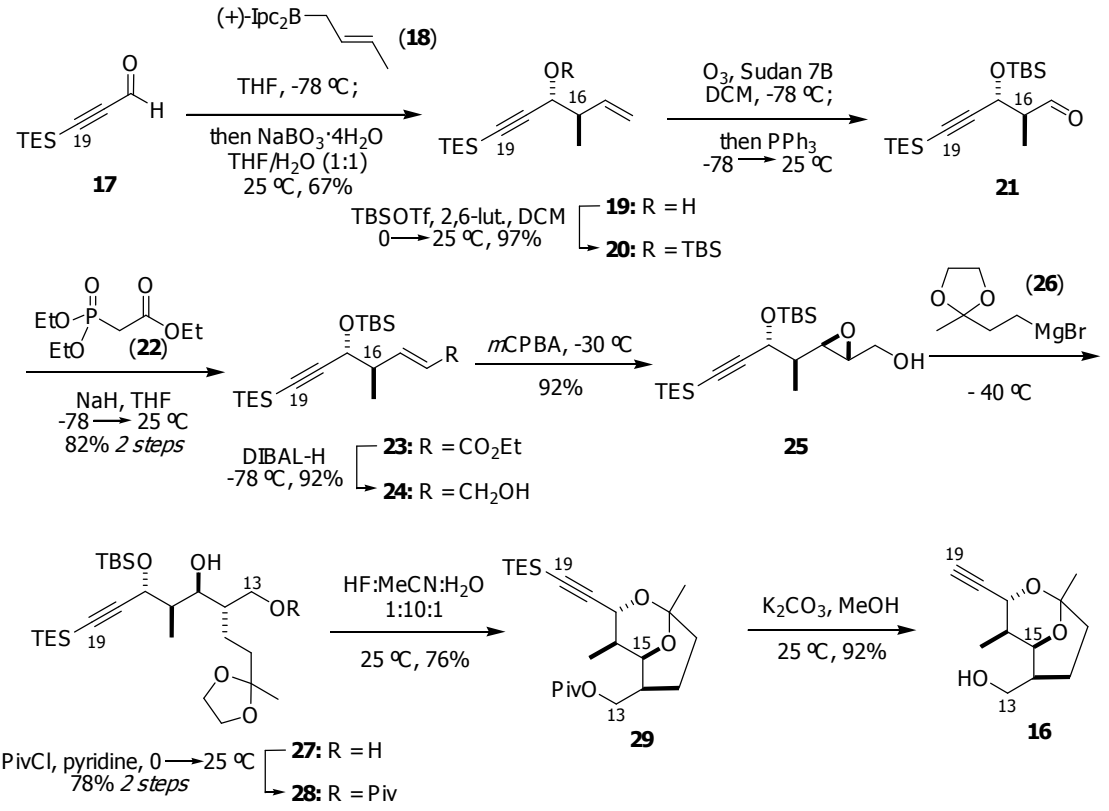
group in **12** was removed by palladium-catalyzed hydrogenolysis to produce primary alcohol **13** which was oxidized to aldehyde **14** using tetrapropylammonium perruthenate in the presence of *N*-methylmorpholine-*N*-oxide.[15] Aldehyde **14** was subjected to homologation using Ohira-Bestmann reagent (**15**)[16] in the presence of potassium carbonate to deliver acetylenic ketal **16**. The pivaloate group was also removed during this process when an excess of potassium carbonate was added.



Scheme 2.1 Nicolaou's synthesis of actylenic ketal **16** (32% yield, *11 steps*)

2.1.2 Alternative Synthesis of the C13-C19 Acetylenic Ketal

A subsequent synthesis of the C13-C19 acetylenic ketal **16** by Nicolaou and coworkers which had the advantage of one less step but no increase in yield is depicted in Scheme 2.2. Subjection of propagylic aldehyde **17**[17] to asymmetric crotylboration[18] with **18** gave alcohol **19** which was protected as *tert*-butyldimethylsilyl ether **20**. After oxidative cleavage of alkene **20** with ozone, the resulting aldehyde **21** was converted to α,β-unsaturated ester **23** via Horner-Wadsworth-Emmons olefination with phosphonate **22**. Reduction of ester **23** with diisobutylaluminum hydride furnished allylic alcohol **24** which was epoxidized with *m*-chloroperoxybenzoic acid to give epoxide **25** with a β:α ratio of ~79:21. Regioselective opening of **25** with Grignard reagent **26**[19] gave diol **27** in which the primary hydroxyl group was protected as pivaloate ester **28**. Removal of the *tert*-butyldimethylsilyl group from **28** with hydrofluoric acid was accompanied by transketalization and furnished ketal **29**. The triethylsilyl and pivaloyl protecting groups were removed with potassium carbonate to complete a second sequence to alkyne **16**.



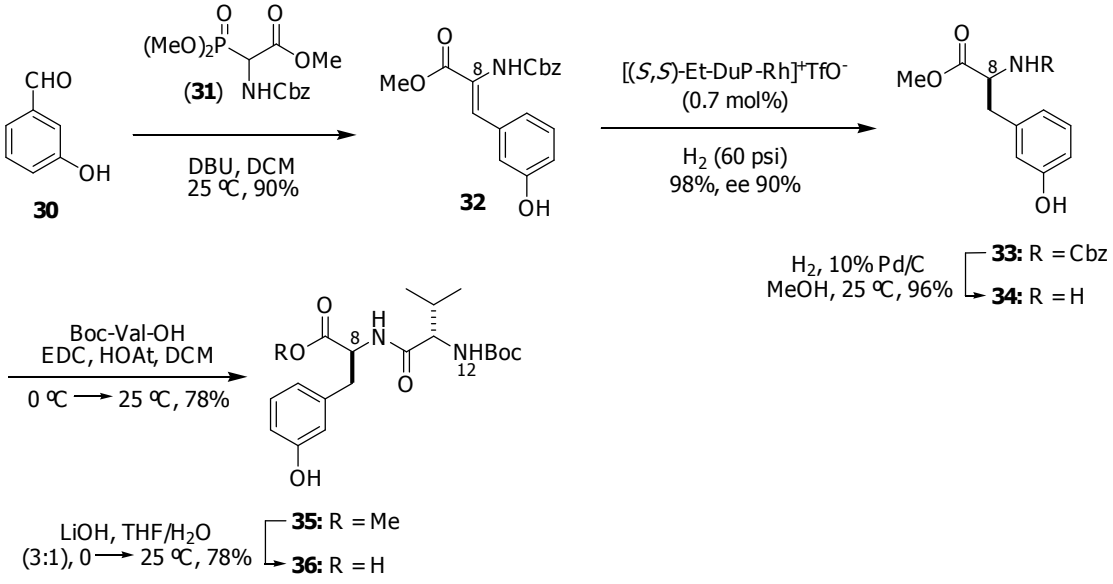
Scheme 2.2 Nicolaou's second synthesis of alkyne **16**

(25% yield, *10 steps*)

2.1.3 Synthesis of the Tripeptide Fragment 44 *via* Enantioselective Hydrogenation and Peptide Coupling

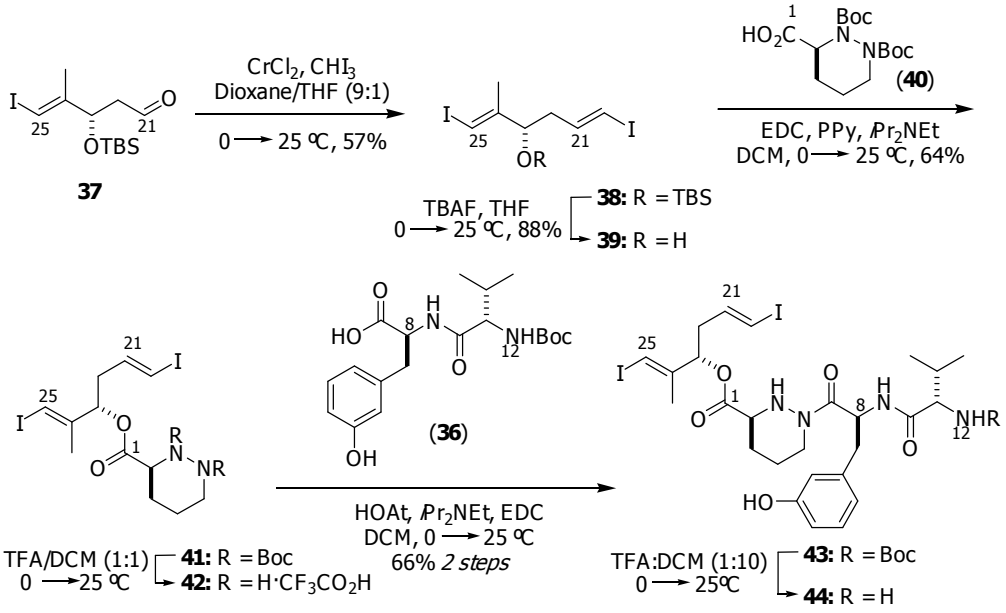
Nicolaou's synthesis of tripeptide fragment **44** began with the stereoselective assembly of the intermediate dipeptide carboxylic acid derivative **36** as depicted in Scheme 2.3. Enantioselective hydrogenation of the *α,β*-dehydroamino acid derivative **32** was the key to construction of the stereocenter at C8. Thus, *N*-benzyloxycarbonylglycine phosphonate **31** was condensed with *m*-

hydroxybenzaldehyde (**30**) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to provide *(Z)*-**32** in excellent yield.[20] Ester **32** was subjected to asymmetric hydrogenation[21] in the presence of rhodium(I) catalyst to afford amino acid derivative **33** with excellent enantiomeric excess and yield. The carbobenzyloxy protecting group in **33** was removed by palladium(0)-catalyzed hydrogenolysis to yield **34** which was coupled with *N*-(*tert*-butoxycarbonyl)-L-valine in the presence of 1-hydroxyl-7-azabenzotriazole to give dipeptide derivative **35**. Finally, hydrolysis of **35** by treatment with lithium hydroxide furnished dipeptide carboxylic acid derivative **36** in good yield.



Scheme 2.3 Nicolaou's synthesis of dipeptide **36** *via* enantioselective hydrogenation (52% yield, *5 steps*)

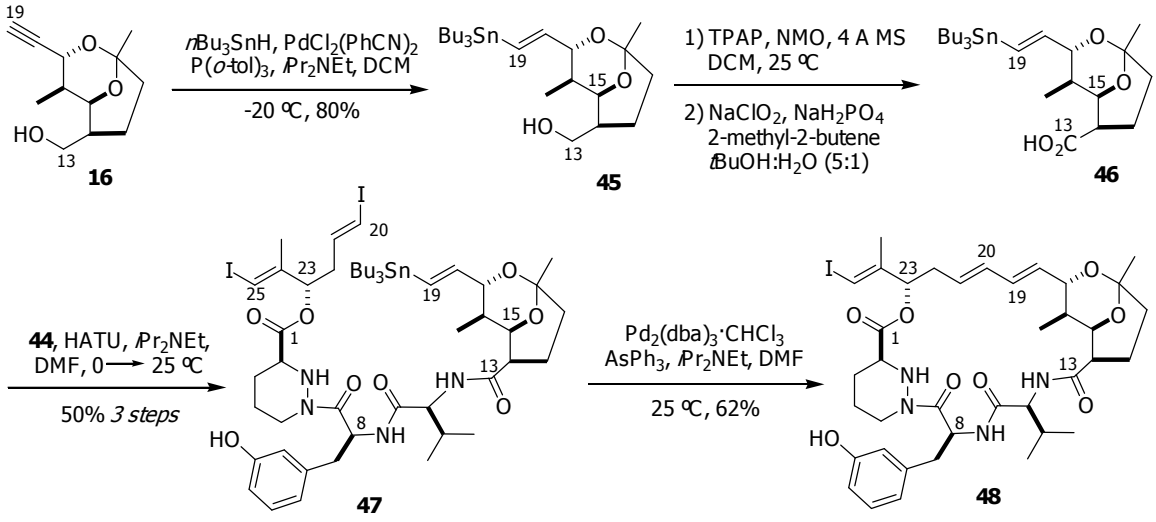
The next task was to prepare diiododiene **39** from known iodo aldehyde **37**[22] as shown in Scheme 2.4. A chromium(II)-mediated Takai reaction[23] was used for stereoselective introduction of the C20-C21 *(E)*-vinyl iodide, after which the *tert*-butyldimethylsilyl ether at C23 of the resulting iodide **38** was unmasked with tetra-*n*-butylammonium fluoride to produce secondary alcohol **39**. Coupling of **39** with *N*,*N*,-di-*tert*-butoxycarbonylpiperazic acid derivative **40**[24] in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and 4-pyrrolidinopyridine provided ester **41**, from which both *tert*-butoxycarbonyl groups were removed upon treatment with trifluoroacetic acid to afford ester **42**. Regioselective amide formation of **42** with dipeptide carboxylic acid derivative **36** in the presence of 1-ethyl-3-(3-dimethylamino propyl)carbodiimide and 1-hydroxyl-7-azabenzotriazole delivered tripeptide ester **43** which was deprotected with trifluoroacetic acid to furnish tripeptide fragment **44**.



Scheme 2.4 Nicolaou's route to tripeptide fragment **44** (19% yield, *6 steps*)

2.1.4 Synthesis of the SFA Macrocyclic Core 48 *via* Intramolecular Stille Coupling

Nicolaou's synthesis of the fully functionalized macrocyclic core of sanglifehrin A (**1**) commenced with the synthesis of vinylstannane **46** from alkyne **16** in three steps as outlined in Scheme 2.5. Thus, alkyne **16** was subjected to palladium(0)-mediated hydrostannylation[25] to give vinylstannane **45** which was oxidized in two steps to carboxylic acid **46**. Peptide coupling of **46** with tripeptide **44** provided the precursor **47** for macrocyclization. Synthesis of macrocycle **48** was completed by treatment of **47** with a palladium(0) catalyst in the presence of Hunig's base to give **48**.

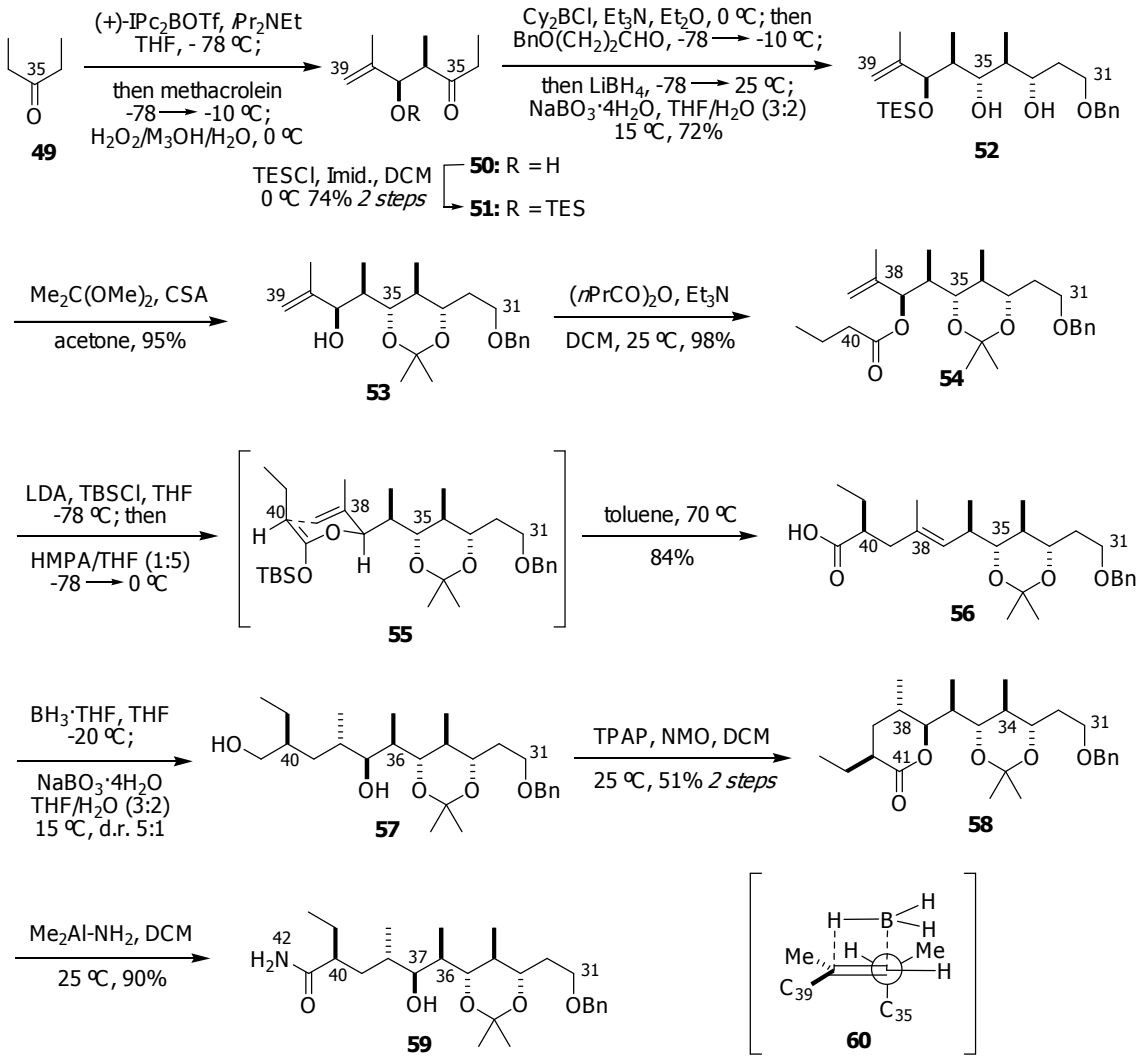


Scheme 2.5 Nicolaou's synthesis of macrocycle **48** (25% yield, *5 steps*)

2.1.5 Synthesis of the Spirolactam Fragment 77 of SFA: Elaboration of the C31-N42 Fragment to Complete the Western Subunit of SFA

Nicolaou's synthesis of the spirolactam **77** began with assembly of the key C31-N42 fragment, amide **59** (Scheme 2.6), which possesses six of the requisite seven stereocenters (C37 alcohol stereochemistry was inconsequential since a ketone functional group was introduced at this carbon in a later step). Asymmetric aldol methodology[26] and substrate-controlled hydroboration were used to install the array of alternating oxygenated and methyl substituted carbons on the C33-C38 backbone, and an Ireland-Claisen rearrangement[27] was employed to introduce the C40 stereocenter. Thus, subjection of diethyl ketone **49** to (+)-diisopinocampheylboron triflate and Hunig's base to generate the corresponding *(Z)*-boron enolate[28] followed by aldol reaction with methacrolein provided secondary alcohol **50**. Protection of **50** as its triethylsilyl ether furnished ketone **51** which underwent a second asymmetric aldol reaction with 3-benzyloxypropanal in the presence of chlorodicyclohexylborane and triethylamine to give an intermediate that was reduced in situ by lithium borohydride to deliver diol **52**. The requisite Ireland-Claisen precursor, ester **54**, was prepared in two steps from diol **52** by protection as its acetonide with 2,2-dimethoxypropane in the presence of camphorsulfonic acid, a process that was accompanied by unmasking of the C37-hydroxyl group to furnish hydroxyacetonide **53**. Acylation of **53** with butyric anhydride in the presence of triethylamine gave **54**. Ester **54** underwent enolization and silylation to generate ketene acetal **55** which upon thermolysis in toluene followed by hydrolysis of the resulting silyl ester afforded carboxylic acid **56** in excellent yield

and as a single diastereoisomer. Carboxylic acid **56** was subjected to substrated-controlled hydroboration followed by an oxidative workup to provide a ~5:1 mixture of diastereomeric diols in favor of the desired stereoisomer **57**. The configurational assignments to C37 and C38 were based on Houk's transition-state model[29] in which the largest group on the chiral center flanking the double bond in **56** is placed anti to the attacking borane so that allylic 1,3-strain is minimized, as illustrated in transition state **60**. Oxidation of diol **57** with tetrapropylammonium perruthenate and *N*-methylmorpholine-*N*-oxide [15] led to lactone **58**, and final treatment of **58** with dimethylaluminum amide[30] afforded acetonide amide **59**.

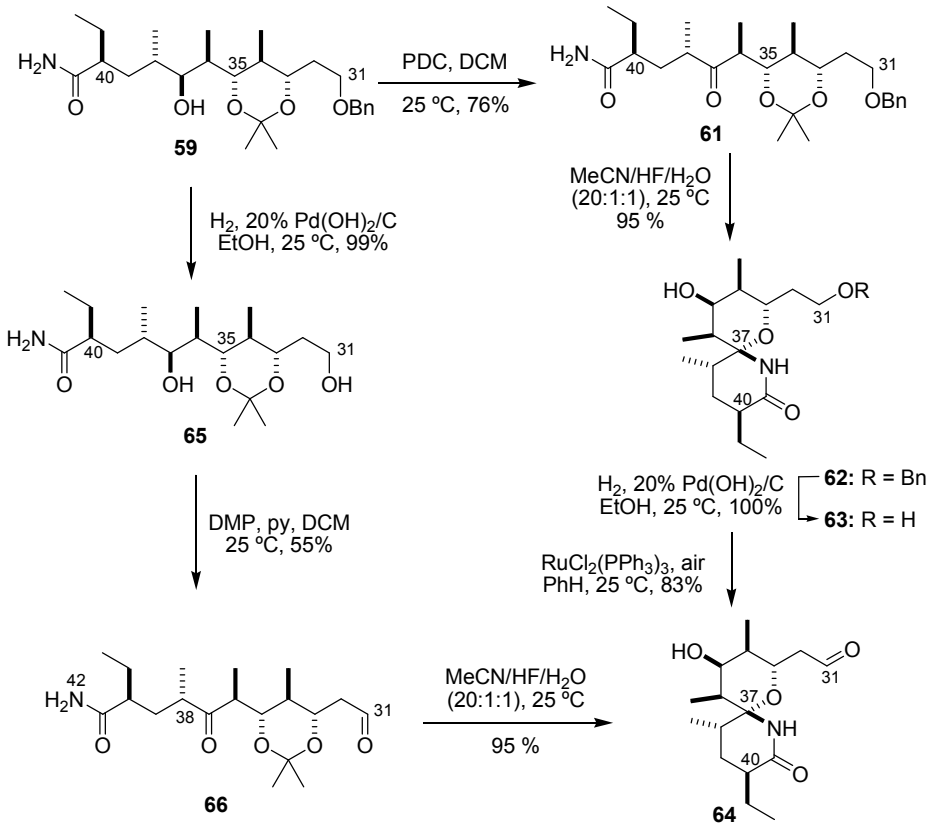


Scheme 2.6 Nicolaou's synthesis of C31-N42 amide fragment **59**

(19% yield, *9 steps*)

With subunit **59** completed, Nicolaou's next task was elaboration of this amide into spirolactam **64**. Two routes to **64** were pursued and are depicted in Scheme 2.7. In the first approach, **59** was converted to keto amide **61** by oxidation with pyridinium dichromate. Hydrolysis of acetonide **61** by hydrofluoric acid in aqueous acetonitrile

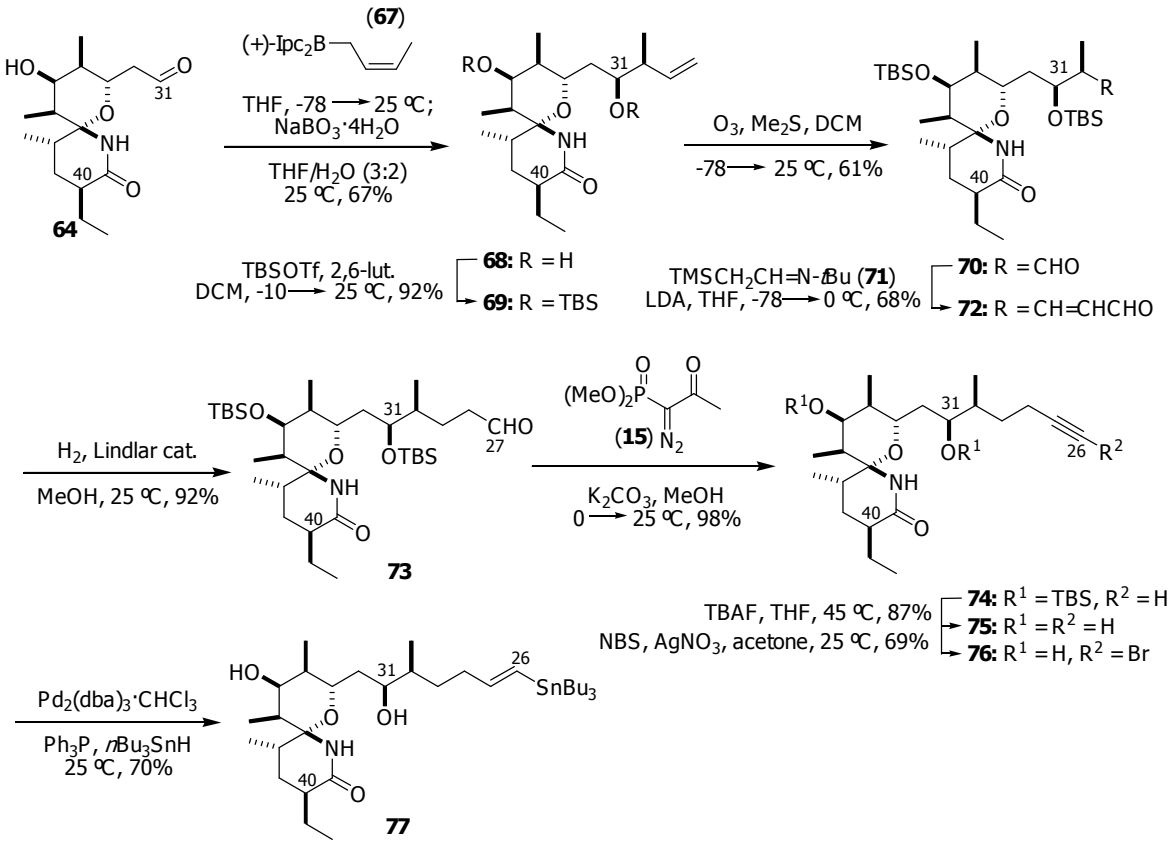
was accompanied by spirocyclization to provide spirolactam **62** in excellent yield; palladium-catalyzed hydrogenolysis of benzyl ether **62** then led to diol **63**. Chemoselective oxidation of the primary hydroxyl group of **63** with oxygen in the presence of a ruthenium(II) catalyst[31] afforded aldehyde **64**. In a shorter sequence leading to **64**, the benzyl ether of **59** was cleaved by catalytic hydrogenolysis and this was followed by oxidation of the resulting diol **65** with Dess-Martin periodinane[32] to give keto aldehyde **66**. Acid-induced spirocyclization of **66** then delivered **64** in excellent yield.



Scheme 2.7 Nicolaou's two approaches to spirolactam aldehyde **64**

(Left 52% yield, *3 steps*; Right 60% yield, *4 steps*)

Completion of Nicolaou's synthesis of the fully functionalized western portion of sanglifehrin A is depicted in Scheme 2.8. Crotylboration of spirolactam aldehyde **64** with **67** furnished homoallylic alcohol **68** as a 7:3 mixture of diastereoisomers. Treatment of **68** with *tert*-butyldimethylsilyl trifluoromethanesulfonate in the presence of 2,6-lutidine gave **69** which was ozonolyzed to provide aldehyde **70**. A two-carbon homologation of **70** to aldehyde **73** was achieved by treatment of the former with the lithio derivative of silyl aldimine **71**[33] to give **72**, after which the double bond of **72** was hydrogenated using Lindlar's catalyst.[34] Aldehyde **73** was transformed into alkyne **74** in excellent yield with Ohira's reagent **15** and subsequent desilylation of both silyl ethers in **74** with tetra-*n*-butylammonium fluoride gave diol **75**. The terminal alkyne of **75** was converted to alkynyl bromide **76** with *N*-bromosuccinimide in the presence of silver nitrate,[35] and treatment of **76** with tri-*n*-butyltin hydride in the presence of in situ-generated catalytic tetrakis(triphenylphosphine)palladium(0) led to vinylstannane **77**.



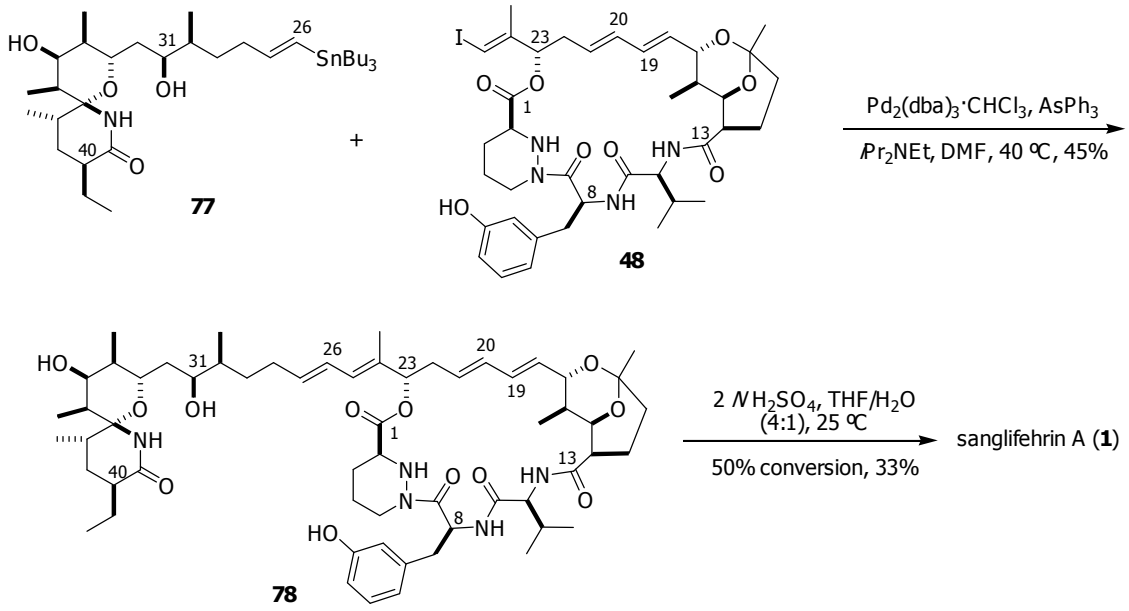
Scheme 2.8 Nicolaou's synthesis of vinylstannane **77**

(10% yield, *9 steps*)

2.1.6 Completion of Nicolaou's Synthesis of Sanglifehrin A Using Stille Coupling to Connect Eastern and Western Segments

Completion of Nicolaou's total synthesis of SFA is shown in Scheme 2.9. Treatment of a mixture of vinylstannane **77** and vinyl iodide **48** with a catalytic amount of in situ-generated tris(triphenylarsine)palladium(0)[36] in *N*,*N*-dimethylformamide at 40 °C delivered sanglifehrin A internal ketal **78** which upon

exposure to aqueous sulfuric acid provided **1**. Nicolaou's synthesis of sanglifehrin A required 49 steps with the longest linear sequence being 23 steps.



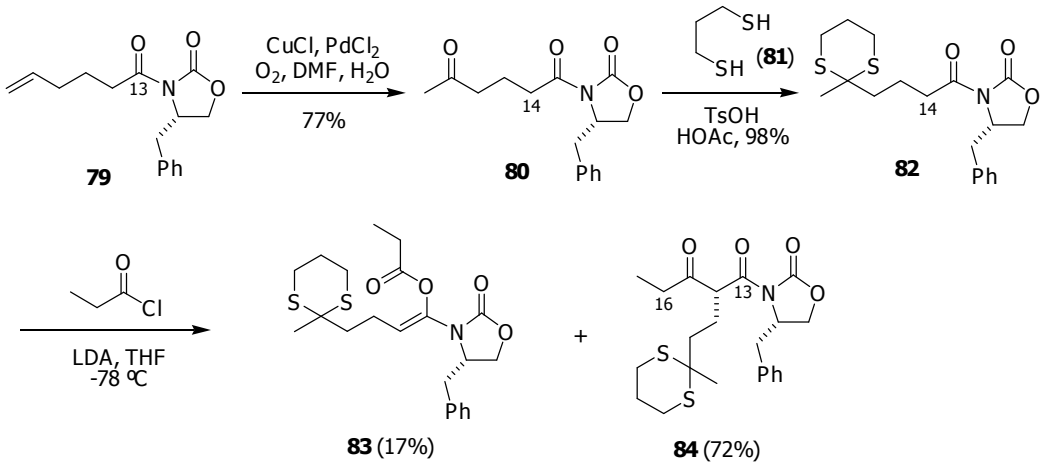
Scheme 2.9 Completion of Nicolaou's synthesis of sanglifehrin A (15% yield, *2 steps*)

2.2 Paquette's Total Synthesis of Sanglifehrin A (2002)

2.2.1 Synthesis of the C13-C16 Fragment *via* Asymmetric Acylation

Paquette's synthesis of the C13-C16 fragment is depicted in Scheme 2.10. Wacker oxidation of the enantiopure oxazolidinone **79**[37] led to regiospecific introduction of a ketone group in **80**, which was converted into dithioketal **82** by treatment with 1,3-propanedithiol (**81**) in the presence of *p*-toluenesulfonic acid. The propionyl substituent in **84** was installed by kinetically controlled attack on the lithium

enolate of **82** with propionyl chloride. This process proceeded with high diastereoselectivity to give principally **84** in combination with *O*-acylation product **83**.

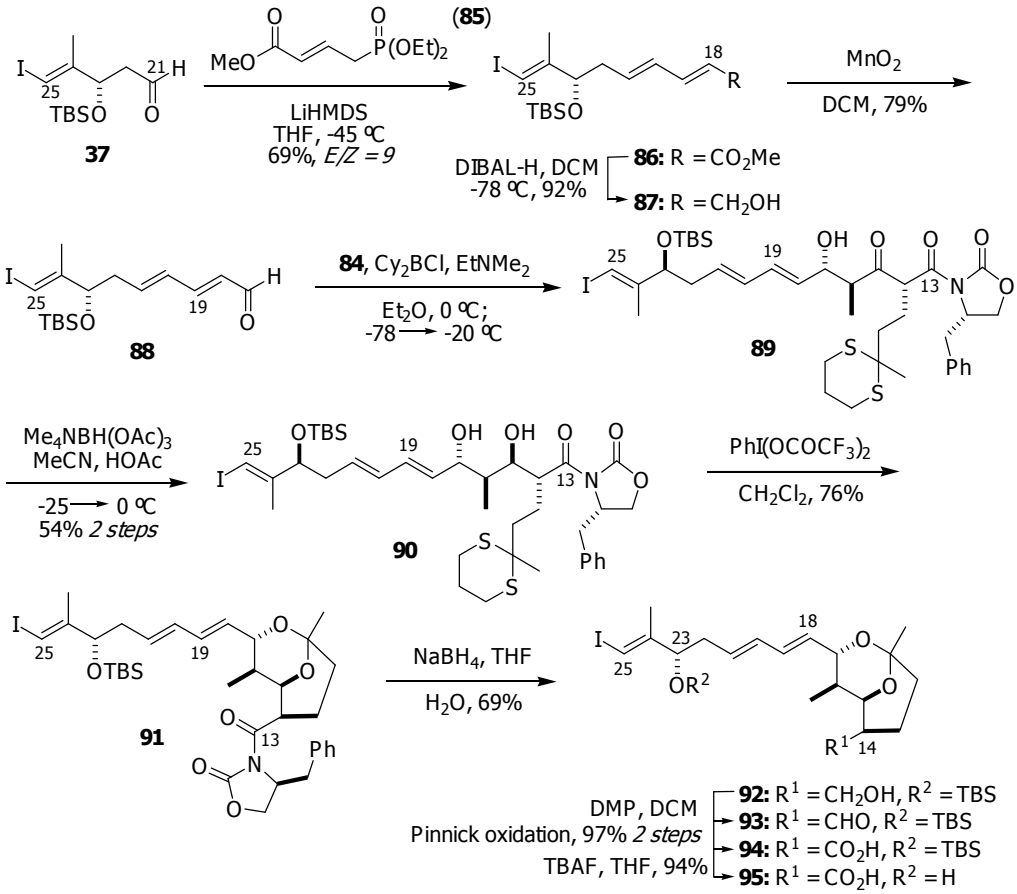


Scheme 2.10 Paquette's synthesis of oxazolidinone **84** (54% yield, *3 steps*)

2.2.2 Synthesis of the C13-C25 Fragment 95 *via* Diastereoselective Anti-Aldol Reaction

Paquette's synthesis of the C13-C25 fragment **95** began with homologation of known aldehyde **37**[22] with phosphonate **85** which led to *α,β,γ,δ*-unsaturated ester **86** as shown in scheme 2.11. Thus, coupling of **37** with the lithium salt of **85** installed the dienyl ester functionality of **86** as a 9:1 mixture in favor of the desired *(E,E)*-isomer **86**. Subsequent reduction of the ester moiety to a primary alcohol with diisobutylaluminum hydride provided allylic alcohol **87** which upon oxidation with manganese dioxide furnished aldehyde **88**. Subjection of aldehyde **88** and the *(E)*-boron enolate of **84** to an asymmetric anti-aldol coupling[38] gave ketone **89** which was reduced stereoselectively with tetramethylammonium triacetoxyborohydride in the

presence of acetic acid to afford diol **90**. Removal of the dithioacetal protecting group from **90** with [bis(trifluoroacetoxy)iodo]benzene was accompanied by internal ketalization to yield **91**. Reductive cleavage of the oxazolidinone of **91** with sodium borohydride in aqueous tetrahydrofuran gave alcohol **92**;[39] Dess-Martin oxidation of this alcohol then gave aldehyde **93** which was further oxidized using Pinnick's conditions to provide carboxylic acid **94**. Finally, the C23-hydroxyl group of **94** was unmasked with tetra-*n*-butylammonium fluoride to afford hydroxy carboxylic acid **95**.

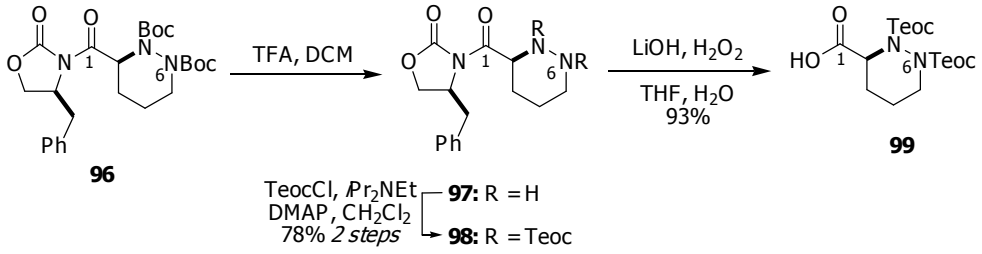


Scheme 2.11 Paquette's synthesis of hydroxy carboxylic acid **95**

(13% yield, *10 steps*)

2.2.3 Paquette's First Generation Approach to Macrocycle 48

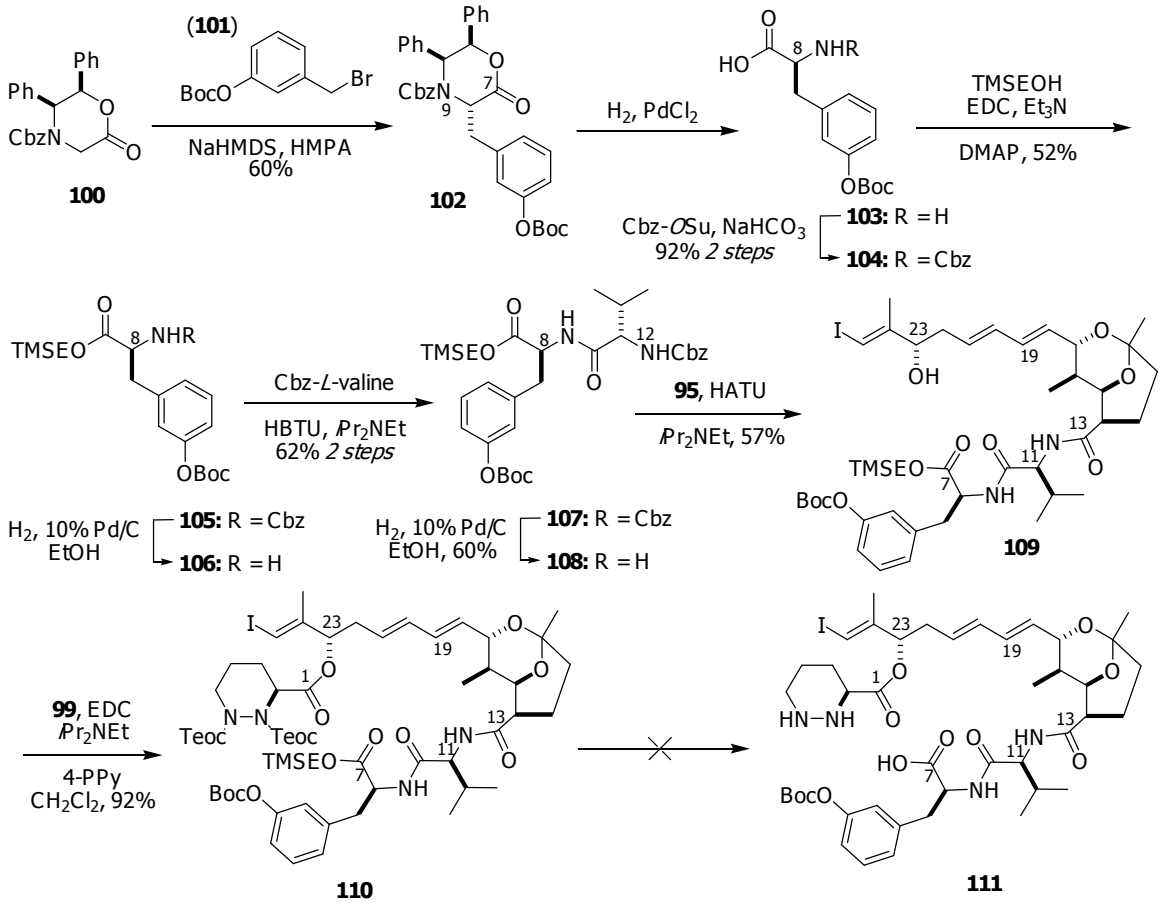
Paquette's initial route to the macrocyclic core **48** of SFA commenced with the synthesis of piperazic acid derivative **99** as outlined in Scheme 2.12. The 2-(trimethylsilyl)ethoxylcarbonyl (Teoc) protecting group[40] was installed on the two piperazic acid nitrogen atoms in the known compound **96**.[41] Thus, both *tert*-butoxycarbonyl protecting groups were removed from **96** under acidic conditions to give **97** and the free diamine **97** was then re-protected with 2-(trimethylsilyl) ethoxycarbonyl chloride in the presence of 4-dimethylaminopyridine to afford **98**. The oxazolidinone chiral auxiliary in **98** was removed under basic conditions, leading to the required piperazic acid derivative **99**. Paquette's reasoning for exchanging the *tert*-butoxycarbonyl groups in **96** for 2-(trimethylsilyl)ethoxycarbonyl protecting groups in **99** was that eventual removal of the latter would be more facile, as has been proven in peptide chemistry[42, 43] and in other settings involving highly functionalized, structurally complex intermediates.[44, 45]



Scheme 2.12 Paquette's synthesis of piperazic acid derivative **99**

(73% yield, *3 steps*)

The next synthetic operation was enantioselective synthesis of *m*-hydroxyphenylalanine derivative **103**, as shown in Scheme 2.13. Commercially available oxazinone **100** was subjected to stereoselective alkylation with benzyl bromide **101** in the presence of hexamethylphosphoramide to deliver **102**, which underwent hydrogenolysis in the presence of dichloropalladium(II) to liberate amino and carboxyl groups and furnish *O*-Boc-hydroxyphenylalanine **103**. Protection of the free amino group in **103** with *N*-(benzyloxycarbonyloxy)succinimide to give **104** was followed by esterification with trimethylsilylethanol in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide to produce **105** in moderate yield. The amino group was unmasked by hydrogenolysis and amino ester **106** was coupled with *N*-carboxybenzyl-L-valine in the presence of *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate to yield dipeptide **107**. Dipeptide **107** was transformed into vinyl iodide **109** in two steps that included deprotection of the carboxybenzyl group to give **108** and coupling of **108** with carboxylic acid **95**. Alcohol **109** was esterified with piperazic acid derivative **99**[46] in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and 4-pyrrolidinopyridine[47] to deliver **110**. However, attempts at removal of the 2-(trimethylsilyl)ethoxycarbonyl and 2-(trimethylsilyl)ethyl groups gave uncharacterizable products and this route to **111** was therefore abandoned.



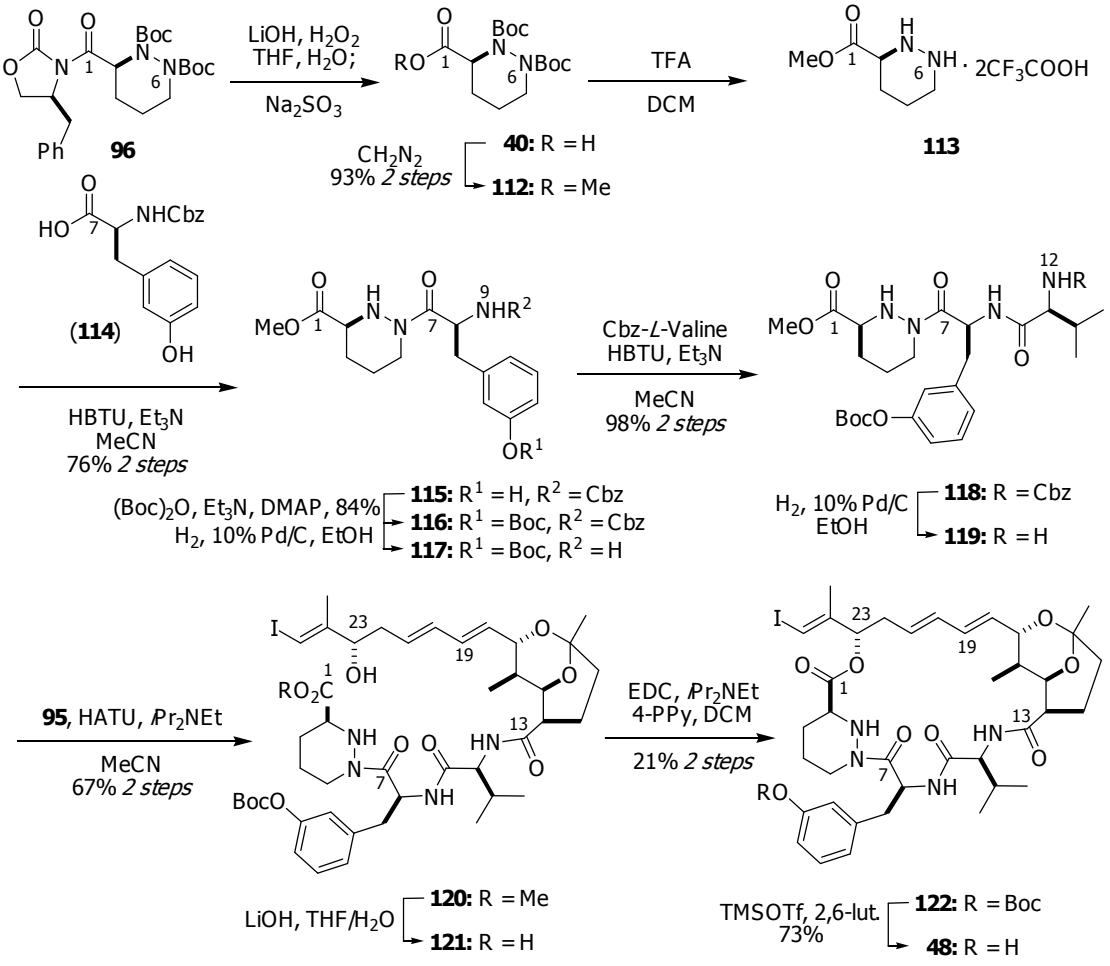
Scheme 2.13 Synthesis of macrocyclization precursor **110**

(6% yield, *9 steps*)

2.2.3 Paquette's Second Generation Approach to Macrocycle 48

Paquette's failure to remove protecting groups from **110** led to a second approach route to macrolactone **48** depicted in Scheme 2.14. In this approach, the focus was on macrolactonization to close hydroxy acid **121**. This plan required access to tripeptide **119**, for which known oxazolidinone **96**[41] was again the starting point. The latter was transformed into piperazic methyl ester **113** in three steps according to

Hale's procedure. First, **96** was cleaved to carboxylic acid **40** which was treated with diazomethane to give methyl ester **112**. The *tert*-butoxylcarbonyl groups were removed from **112** by treatment with trifluoroacetic acid to provide **113**. Peptide coupling of **113** with *m*-tyrosine derivative **114** produced dipeptide **115** in which the phenolic hydroxyl group was protected with *tert*-butoxycarbonyl anhydride to give **116**. The primary amino group of **116** was unmasked by palladium-catalyzed hydrogenolysis to form dipeptide **117** which was coupled with *N*-carbobenzyloxy-L-valine in the presence of *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate to deliver tripeptide **118**. The latter was converted to hydroxy ester **120** in two steps involving hydrogenolytic cleavage of the carbobenzyloxy protecting group at the N-terminus of the tripeptide and then amide formation of the liberated amino group in **119** with carboxylic acid **95** to construct the N12-C13 bond of SFA. The methyl ester in **120** was hydrolyzed under basic conditions to give hydroxy carboxylic acid **121**, the precursor for macrolactonization. Although lactone **122** was produced in low yield when treated with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide in the presence of 4-pyrrolidinopyridine, the phenolic hydroxyl group of **122** was unmasked with trimethylsilyl triflate and 2,6-lutidine to provide a usable quantity of macrocycle **48**. The latter bears a terminal iodoalkene moiety ready for linkage with the western segment of sanglifehrin A.

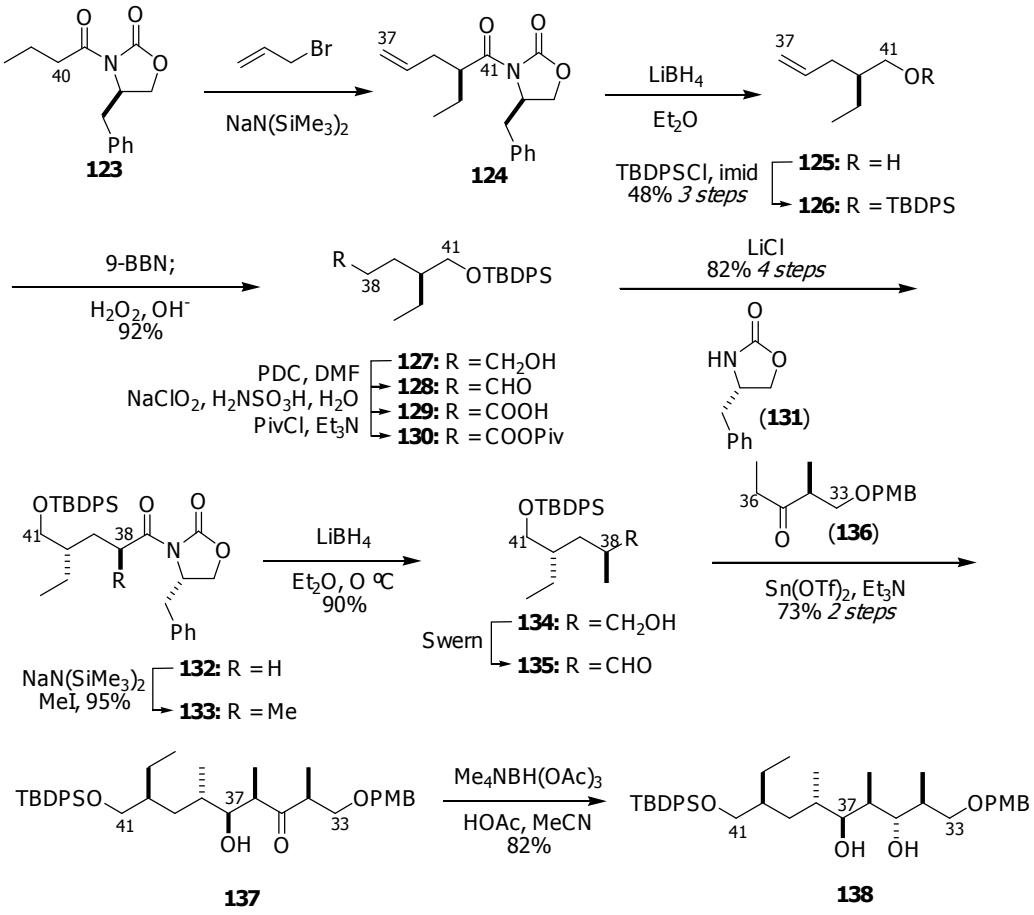


Scheme 2.14 Paquette's synthesis of macrolactone **48** (6% yield, *12 steps*)

2.2.4 Elaboration of the C26-N42 Spirolactam

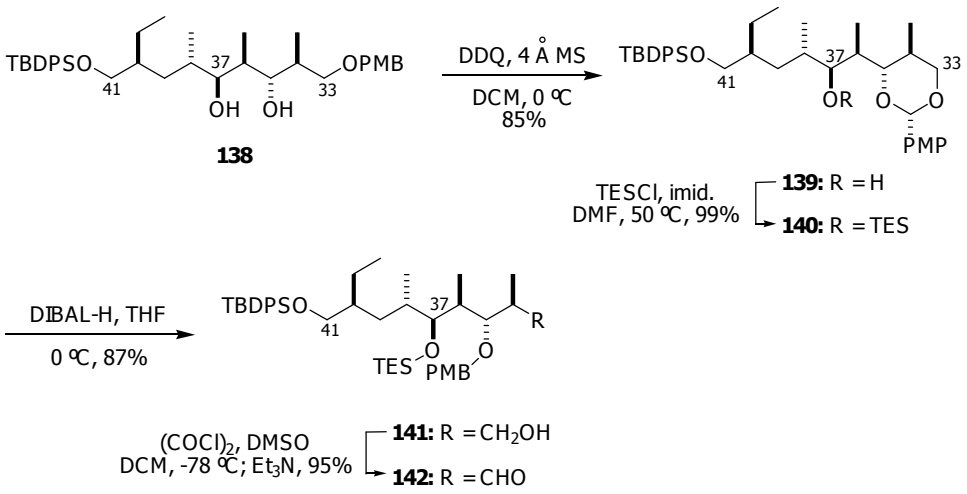
Paquette's synthesis of the C26-N42 spirolactam portion of SFA commenced with asymmetric allylation of known *(R)*-acyloxazolidinone **123** with allyl bromide to produce **124** as shown in Scheme 2.15. The chiral auxiliary was removed from **124** with lithium borohydride in wet ether to furnish alcohol **125** which was protected as its *tert*-butyldiphenylsilyl ether **126**. This alkene was converted to primary alcohol **127**

by hydroboration with 9-borabicyclo[3.3.1]nonane followed by oxidation with basic hydrogen peroxide. Further oxidation of **127** with pyridinium dichromate gave aldehyde **128** which was subjected to Pinnick oxidation to provide carboxylic acid **129**. The acid was advanced to oxazolidinone **132** through adaptation of an activated anhydride protocol[48, 49] in which **129** was transformed into **130** and then condensed with **131** in the presence of lithium chloride. Enantioselective methylation of the enolate of **132** with methyl iodide gave **133**, after which reductive cleavage of the chiral auxiliary with lithium borohydride led to alcohol **134**. Swern oxidation of **134** afforded aldehyde **135** which was condensed with the tin(II) enolate of **136**[50-52] to yield a 92:8 mixture favoring syn,anti diastereomer **137** resulting from Felkin attack. Synthesis of diol **138** was completed by a hydroxyl-directed reduction of **137** with tetramethylammonium triacetoxyborohydride[53]



Scheme 2.15 Paquette's synthesis of diol **138** (19% yield, *13 steps*)

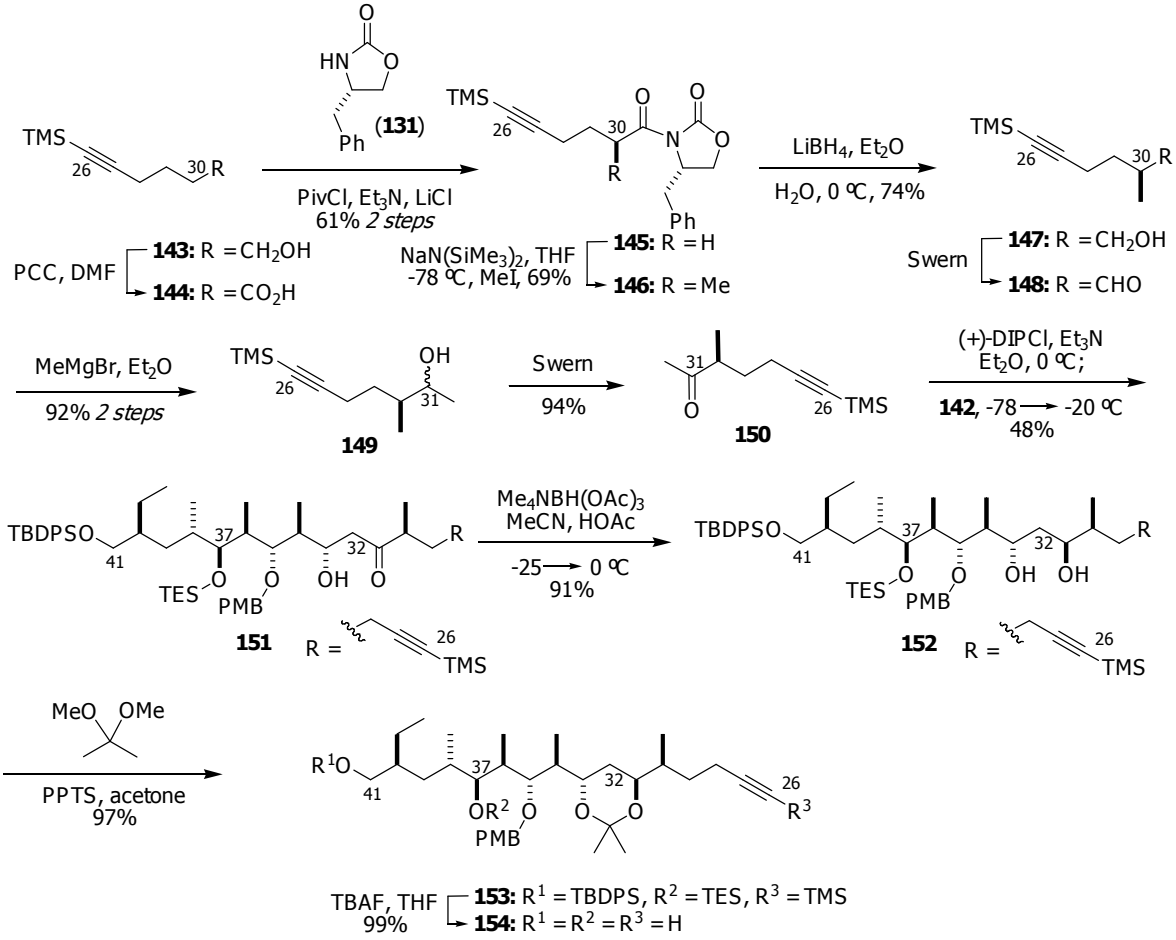
Advancing from diol **138**, Paquette prepared aldehyde **142** required for extension of the carbon framework that would lead to the C26-C41 portion of SFA. Thus, **138** was transformed into terminal *p*-methoxyphenyl acetal **139**[54] in which the remaining hydroxyl group was protected as its triethylsilyl ether **140** (Scheme 2.16). Regioselective reduction of **140** with diisobutylaluminum hydride[55] gave primary alcohol **141** and a subsequent Swern oxidation led to aldehyde **142**.



Scheme 2.16 Paquette's synthesis of aldehyde **142** (70% yield, *4 steps*)

A seven-carbon chain extension of **142** in the direction of C26-C32 of SFA commenced with oxidation of alcohol **143** with pyridinium chlorochromate,[56] activation of the resulting carboxylic acid **144** with pivaloyl chloride, and condensation of the mixed anhydride with oxazolidinone **131** to provide alkyne **145** (Scheme 2.17). Stereoselective methylation of **145** gave **146** from which the chiral auxiliary was cleaved with lithium borohydride in wet ether. This led to alcohol **147** which was oxidized under Swern conditions to aldehyde **148**. A Grignard reaction of **148** with methylmagnesium bromide delivered secondary alcohol **149** which was oxidized to methyl ketone **150**. Linkage of **142** with **150** was effected via an asymmetric aldol reaction employing the chiral enolate of **150** prepared with Lewis-acidic (+)-*B*-chlorodiisopinocampheylborane (DIPCl) in the presence of triethylamine. The ketone of aldol adduct **151** was reduced to give diol **152** by means of a 1,3-anti-selective reduction with tetramethylammonium triacetoxyborohydride in acetic acid.

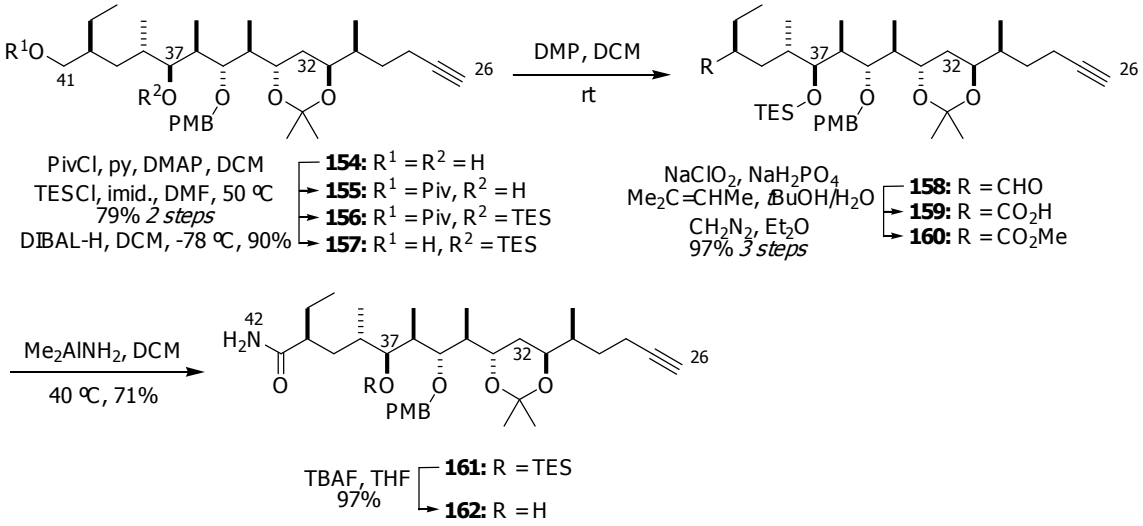
The 1,3-diol in **152** was protected as its acetonide **153** and the three silyl protecting groups in **153** were removed in a single operation with tetra-*n*-butylammonium fluoride to furnish diol **154**.



Scheme 2.17 Paquette's synthesis of diol **154** (12% yield, *11 steps*)

In order to differentiate the two hydroxyl groups in **154**, the primary alcohol was first protected as pivaloate and the remaining hydroxyl group in **155** was then masked as a triethylsilyl ether to produce **156** (Scheme 2.18). Reduction of the primary pivaloate ester in **156** afforded alcohol **157** which was converted to carboxylic

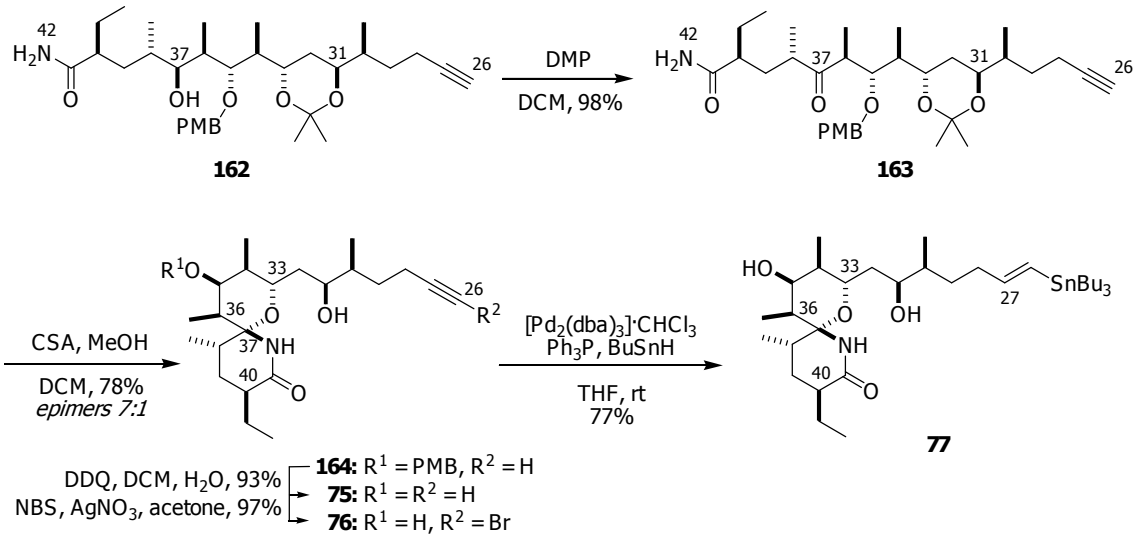
acid **159** via a two-step oxidative sequence through aldehyde **158**. The carboxyl group in **159** was converted to a methyl ester and treatment of **160** with freshly prepared dimethylaluminum amide in dichloromethane at reflux yielded amide **161**.[30] Cleavage of triethylsilyl ether **161** with tetra-*n*-butylammonium fluoride then led to hydroxy amide **162**.



Scheme 2.18 Paquette's route to hydroxy amide **162** (47% yield, *8 steps*)

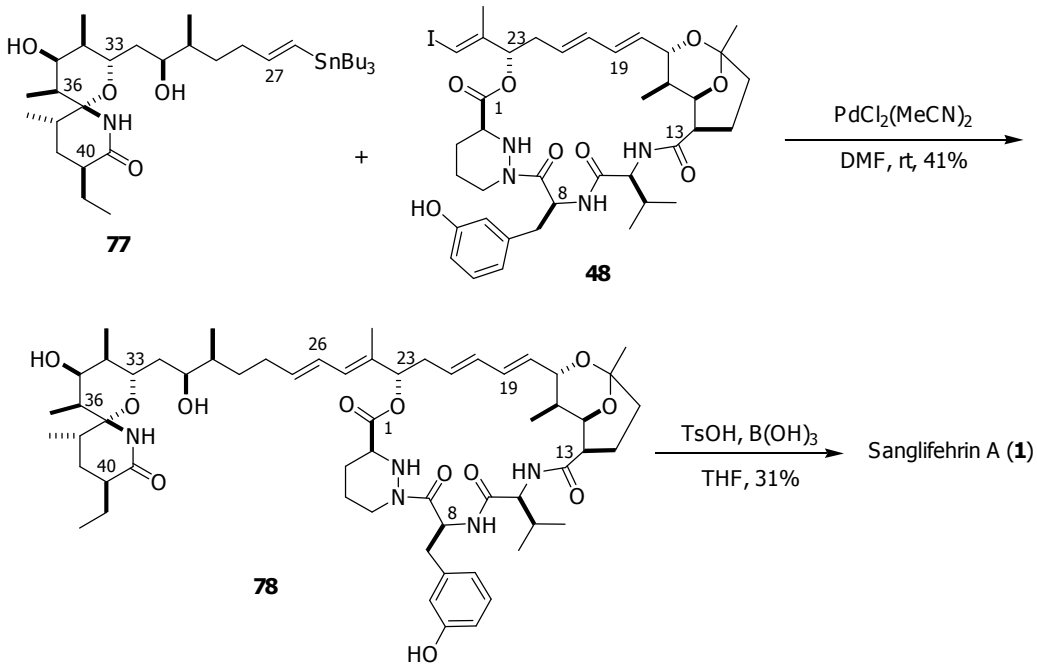
With **162** in hand, Paquette and co-workers advanced toward the C26-N42 spirolactam **77** with oxidation of the C37 hydroxyl group to keto amide **163** (Scheme 2.19). Treatment of **163** with camphorsulfonic acid produced mainly spirolactam **164** along with its spiro (C37) epimer in a 7:1 ratio. After deprotection of the *p*-methoxybenzyl ether in **164**, the resulting alkyne **75** was reacted with *N*-bromosuccinimide in the presence of silver nitrate[35] to provide bromoalkyne **76**. The bromoalkyne was reduced to vinylstannane **77** by reaction with tri-*n*-butyltinhydride,

triphenylphosphine and dipalladium-tris(dibenzylideneacetone)chloroform complex following a protocol due to Guibé.[25]



Scheme 2.19 Paquette's synthesis of spirolactam **77** (53% yield, *5 steps*)

A palladium-catalyzed Stille coupling was chosen for linking C1-C25 subunit **48** with C26-N42 moiety **77** as shown in Scheme 2.20. Thus, treatment of vinylstannane **77** and vinyl iodide **48** with bis(acetonitrile)dichloropalladium(II) in dimethylformamide furnished sanglifehrin A derivative **78**. Finally, the cyclic ketal of **78** was hydrolyzed with *p*-toluenesulfonic acid and boric acid to complete the synthesis of sanglifehrin A. Paquette's synthesis of sanglifehrin A required 68 steps with a longest linear sequence of 35 steps.



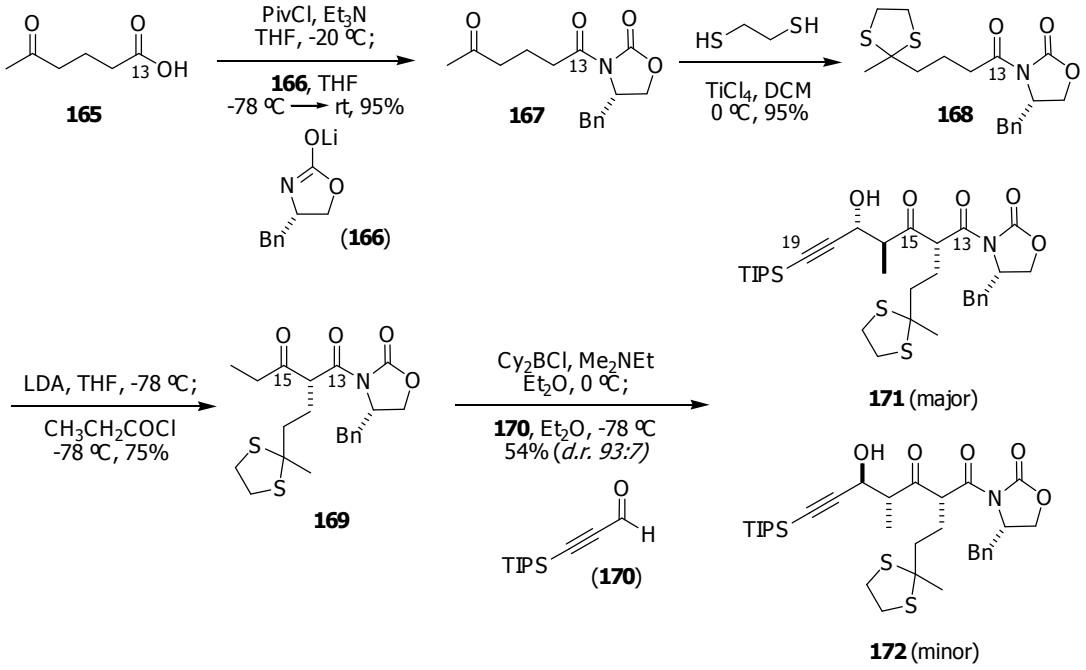
Scheme 2.20 Completion of Paquette's synthesis of sanglifehrin A

(13% yield, *2 steps*)

2.3 Metternich's Synthesis of the C13-C19 Segment of SFA (1999)

Metternich's synthesis of the C13-C19 unit of SFA commenced with the synthesis of alcohol **171**, for which a boron-mediated anti-aldol condensation was employed as a key step. As depicted in Scheme 2.21, commercially available 5-ketohexanoic acid (**165**) was activated as its pivaloyl anhydride which was condensed with lithium enolate **166** to give acyl oxazolidinone **167**.[49] Protection of the keto group of **167** with ethane-1,2-dithiol in the presence of titanium(IV) chloride furnished dithioketal **168** which was subjected to stereoselective acylation with propionyl chloride to yield *β*-ketoimide **169** as a single diastereomer. Treatment of **169** with

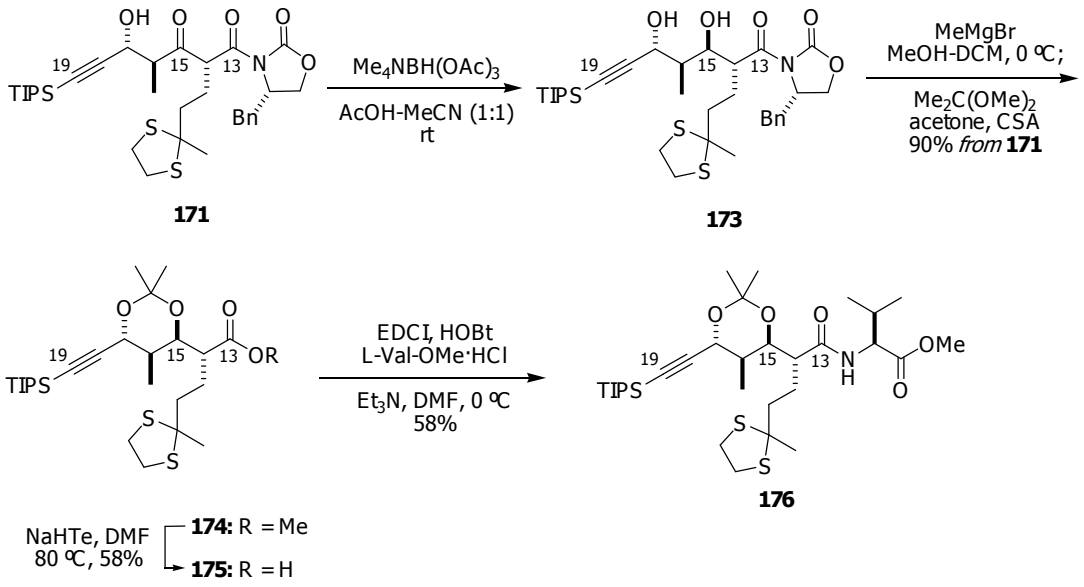
chlorodicyclohexylborane in the presence of ethyldimethylamine generated the *E*-boron enolate of **169** which was condensed with propagylic aldehyde **170** to afford a 93:7 mixture of diastereomers in favor of **171** over **172**.



Scheme 2.21 Metternich's synthesis of alcohol **171** (36% yield, *4 steps*)

Metternich's elaboration of the C13-C19 unit **171** is shown in Scheme 2.22. Stereoselective reduction of the C15-carbonyl group of **171** with tetramethylammonium triacetoxyborohydride gave 1,3-anti diol **173**, after which removal of the chiral auxiliary in **173** with methylmagnesium bromide in methanol/dichloromethane followed by transketalization with 2,2-dimethoxypropane in the presence of camphorsulfonic acid yielded acetonide **174**. The methyl ester of **174** was cleaved with sodium hydrogen telluride in *N*,*N*-dimethylformamide[57] to give carboxylic acid **175**, and peptide coupling of **175** with L-valine methyl ester mediated

by 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and 1-hydroxybenzotriazole delivered amide **176**. This last step was apparently intended as a model for coupling of **175** with the intact C1-N12 tripeptide of SFA. Metternich's synthesis of the tripeptide **187** is described in Section 2.4 below.

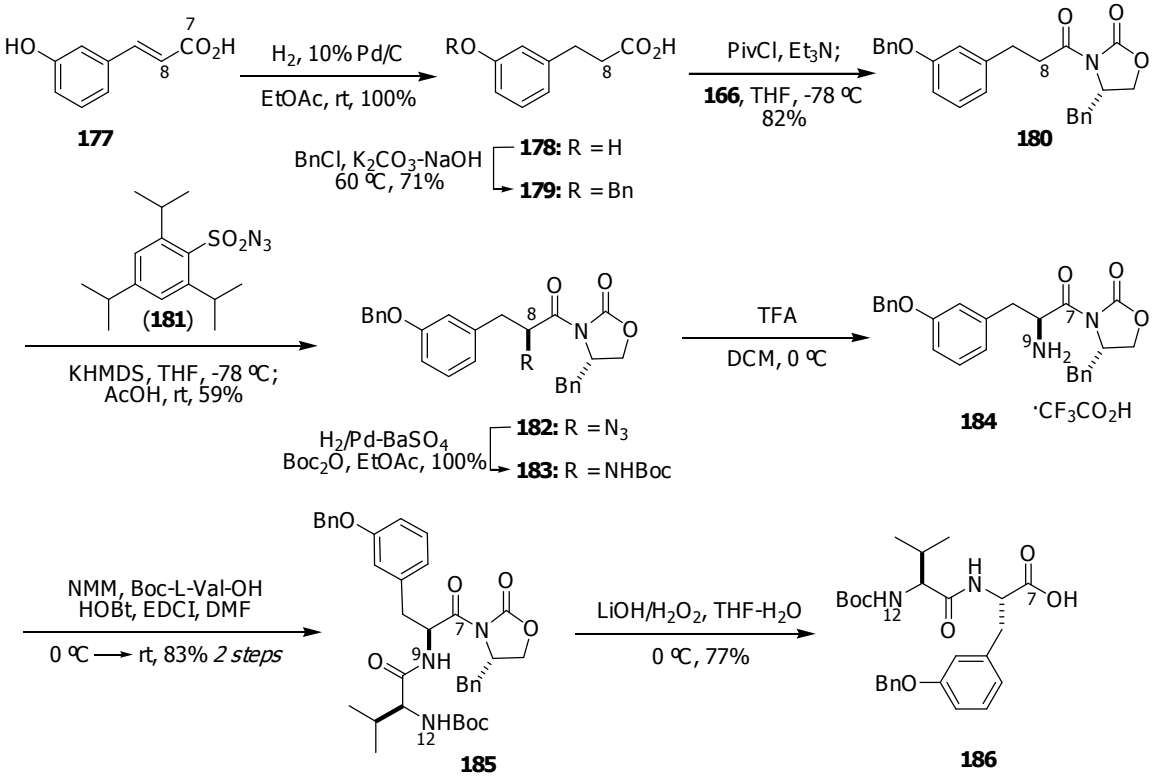


Scheme 2.22 Metternich's synthesis of amide **176** (30 %, *4 steps*)

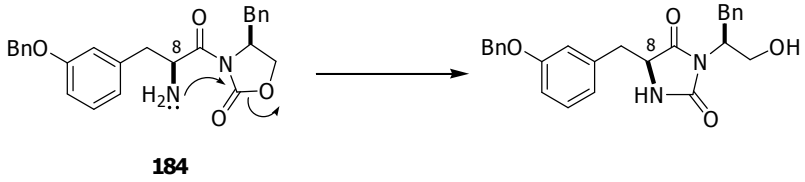
2.4 Metternich's Synthesis of the C1-N12 Tripeptide Subunit of SFA (1999)

Synthesis of the C1-N12 tripeptide component of SFA in Metternich's hands commenced with selective hydrogenation of commercially available 3-hydroxycinnamic acid **177** to give carboxylic acid **178**. The phenolic hydroxy group of **178** was protected with benzyl chloride under basic conditions to yield benzyl ether **179** (Scheme 2.23), and a benzyl oxazolidinone chiral auxiliary was appended to **179**

with lithium enolate **166** using the pivaloyl mixed anhydride method[49] to afford acyl oxazolidinone **180**. The latter underwent stereoselective azide introduction with triisopropylbenzenesulfonyl azide (**181**) to afford azide **182**.[58] Palladium(0)-catalyzed hydrogenation of azide **182** in the presence of barium sulfate and di-*tert*-butyl dicarbonate gave the protected amine **183.** By contrast, catalytic reduction of **182** in the absence of di-*tert*-butyl dicarbonate led to attack on the oxazolidinone by the liberated amine to produce a hydantoin, as illustrated in Scheme 2.24. Removal of the *tert*-butoxycarbonyl group from **183** with trifluoroacetic acid provided amine salt 184 which was coupled with *N*-*tert*-butoxycarbonyl-L-valine using 1-hydroxybenzotriazole and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide[59, 60] in the presence of *N*-methylmorpholine to give the C7-N12 sector of SFA, **185**. Lithium peroxide hydrolysis[61] of **185** in wet tetrahydrofuran delivered carboxylic acid **186** without epimerization of the C7 stereocenter.



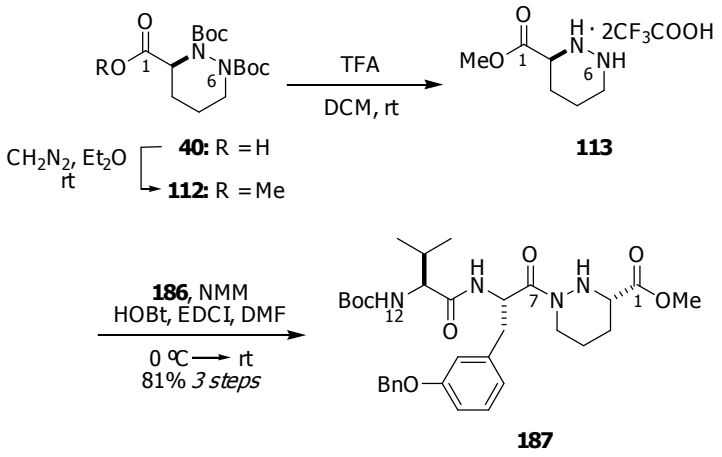
Scheme 2.23 Metternich's synthesis of dipeptide **186** (22% yield, *8 steps*)



Scheme 2.24 Formation of a hydantoin from oxazolidinone **184**

With **186** in hand, Metternich coupled the dipeptide with known piperazic acid derivative **113**[41] to give **187**, the C1-N12 portion of SFA, as shown in Scheme 2.27. First, carboxylic acid **40** was converted to methyl ester **112** and then the pair of *tert*-butoxycarbonyl groups was removed with trifluoroacetic acid to form piperazic acid methyl ester **113**. Peptide coupling of **113** with **186** in the presence of *N*-

methylmorpholine yielded tripeptide **187**. However, no further progress from **175** or **187** towards SFA has been reported from the Metternich laboratory.

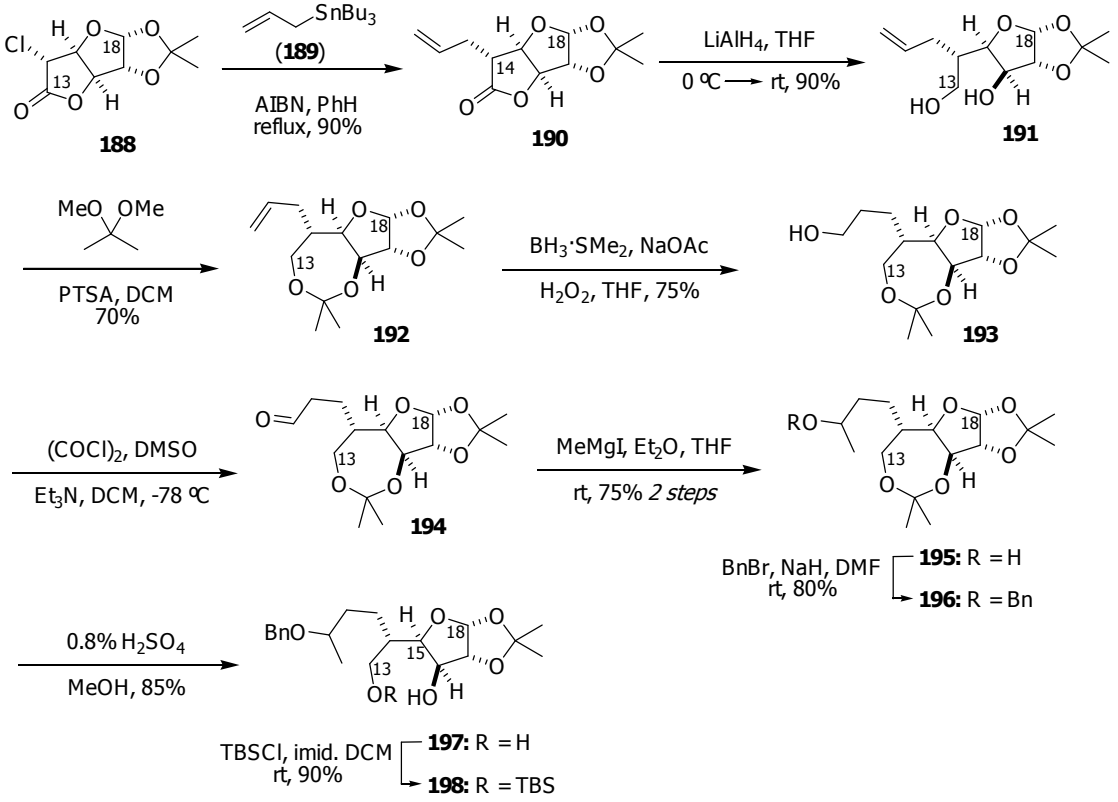


Scheme 2.25 Metternich's synthesis of tripeptide **187** (81% yield, *3 steps*)

2.5 Gurjar's Synthesis of the C13-C18 Segment of SFA (2002)

Gurjar's synthetic route to the C13-C18 portion of SFA began with a stereoselective C-C bond forming reaction through radical mediated coupling of *(5R)-5*-chloro-5-deoxy-glucurono-6,3-lactone derivative **188**[62] with allyltributyltin (**189**), as illustrated in Scheme 2.23. Treatment of **188** with **189** in the presence of azobisisobutyronitrile furnished lactone **190** which was reduced with lithium aluminun hydride to 1,4-diol **191**. Transketalization of **191** with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid afforded acetonide **192**, and this was subjected to a hydroboration-oxidation sequence to produce primary alcohol **193**. Oxidation of **193** under Swern conditions provided aldehyde **194** which was reacted with methylmagnesium iodide to give secondary alcohol **195** as a single diastereomer. The

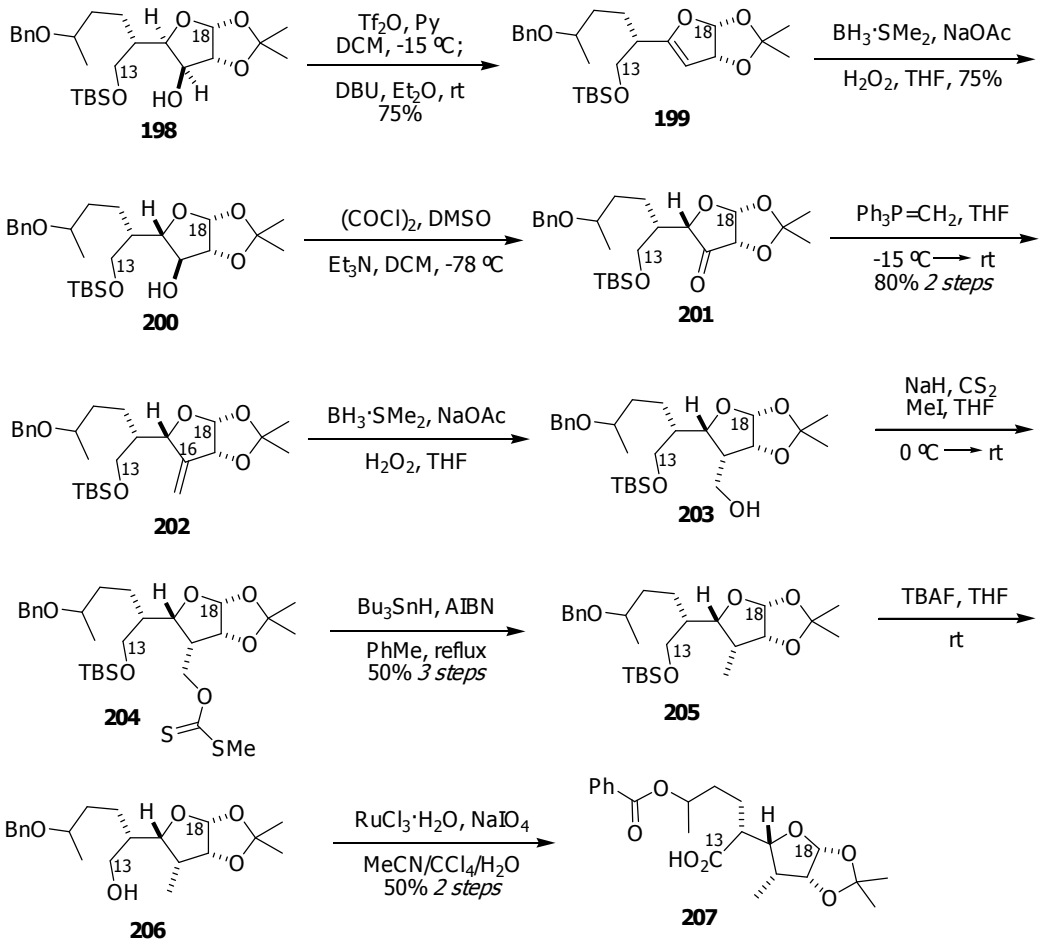
configuration of the new stereo center in **195** was inconsequential as it would later be transformed into a ketone. The secondary hydroxyl group in **195** was protected with benzyl bromide to yield benzyl ether **196** in which the cyclic ketal moiety was cleaved with dilute sulfuric acid to give diol **197**. Silylation of the primary hydroxyl group in **197** with *tert*-butyldimethylsilyl chloride in the presence of imidazole led to **198**.



Scheme 2.26 Gurjar's synthesis of alcohol **198** (20% yield, *9 steps*)

Gurjar's next plan was to invert C15 configuration in **198**, for which elimination of the C16 hydroxyl group to give a dihydrofuran followed by facially selective oxidation, as depicted in Scheme 2.24, was programmed. Thus, alcohol **198** was treated with trifluoromethanesulfonic anhydride in the presence of pyridine and

then with 1,8-diazabicyclo[5.4.0]undec-7-ene to give **199**. Oxidative hydroboration of dihydrofuran **199** yielded alcohol **200** in which attack by borane had occurred at the exo face of the alkene (opposite the acetonide) to give reversed stereochemistry at C15. Oxidation of the secondary alcohol in **200** under Swern conditions furnished ketone **201** which was subjected to Wittig olefination to afford *exo*-methylene derivative **202**. A hydroboration-oxidation sequence was employed to construct the primary alcohol of **203** and set in place the desired C16 stereochemistry. Thus, reaction of **202** with borane-dimethylsulfide complex led to **203** which was transformed into dithiocarbonate **204** in the presence of sodium hydride, carbon disulfide and methyl iodide. Subjection of **204** to Barton radical deoxygenation[63] with tributyltin hydride and azobisisobutyronitrile gave **205**, after which desilylation with tetra-*n*-butylammonium fluoride provided primary alcohol **206**. Ruthenium(III)-mediated oxidation of the primary alcohol in **206** to a carboxylic acid was accompanied by oxidation of the benzyl group to give benzoate **207**. Although carboxylic acid **207** bears all of the functionality needed for the C13-C18 fragment of SFA, Gurjar has not continued his route from this point.

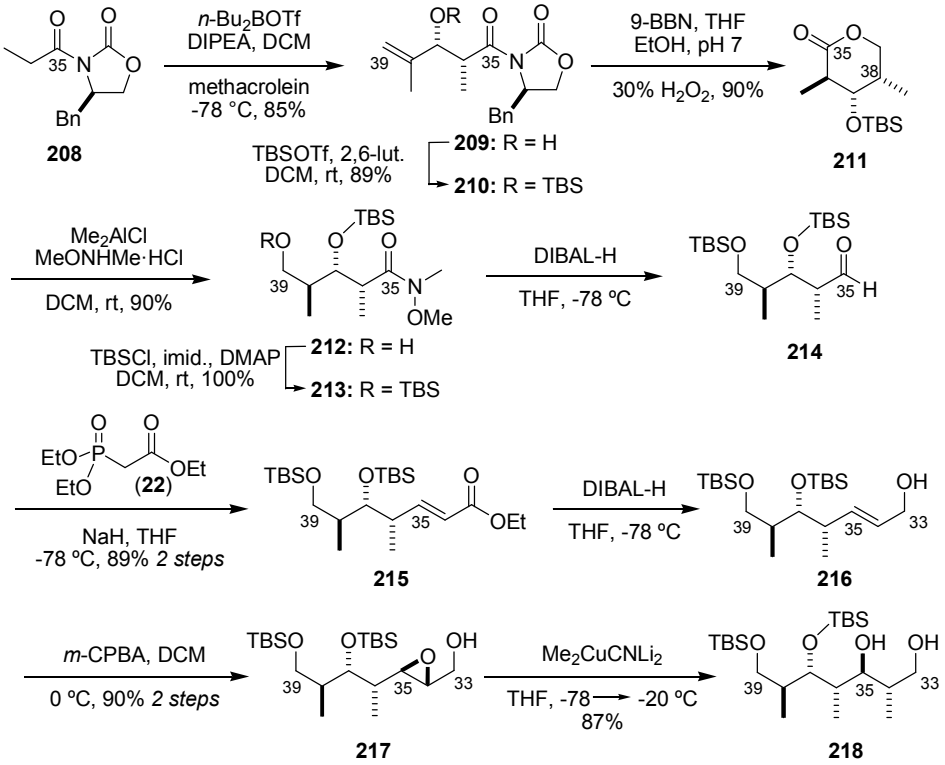


Scheme 2.27 Gurjar's synthesis of carboxylic acid **207** (11% yield, *9 steps*)

2.6 Dias' Synthesis of the C29-C39 Subunit of SFA (2006)

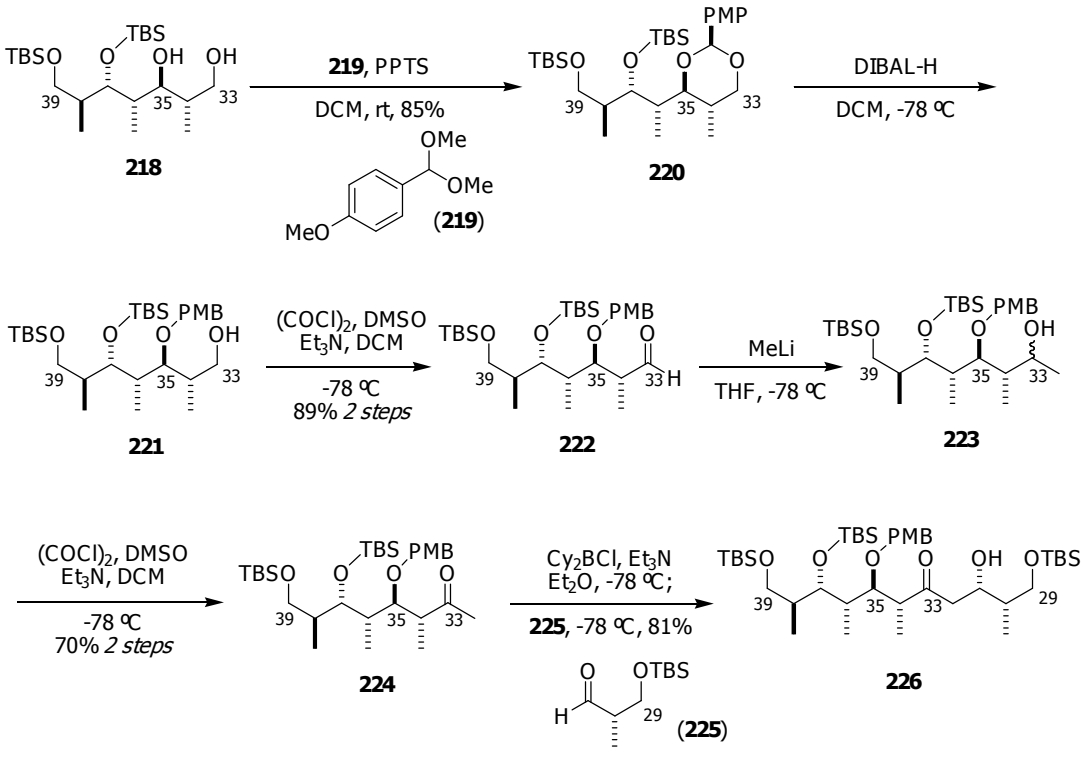
Dias' approach to the C29-C39 portion of SFA began with asymmetric aldol addition of the boron enolate derived from *N*-propionyloxazolidinone **208** to methacrolein. This gave *syn*-aldol adduct **209**,[64-66] after which the new secondary alcohol was protected with *tert*-butyldimethylsilyl triflate in the presence of 2,6-lutidine to yield acyl oxazolidinone **210** (Scheme 2.28). Subjection of **210** to a hydroboration-oxidation sequence with 9-borabicyclo(3.3.1)nonane resulted in

cleavage of the chiral auxiliary and led to lactone **211**. Treatment of **211** with *N,O*-dimethylhydroxylamine hydrochloride in the presence of dimethylaluminum chloride gave Weinreb amide **212**[30, 67, 68] in which the primary alcohol was masked with *tert*-butyldimethylsilyl chloride to afford amide **213**. After reduction with diisobutylaluminum hydride at low temperature, **213** provided aldehyde **214**. Horner-Wadsworth-Emmons olefination[69] of **214** with phosphonate **22** gave *α,β*-unsaturated ester **215** which was reduced with diisobutylaluminum hydride to yield allylic alcohol **216**. Diastereoselective epoxidation of **216** with *m*-chloroperoxybenzoic acid delivered epoxide **217**[70] which underwent opening with lithium dimethylcopper(I) cyanide to give 1,3-diol **218**.[71]



Scheme 2.28 Dias's synthesis of diol **218** (43% yield, *10 steps*)

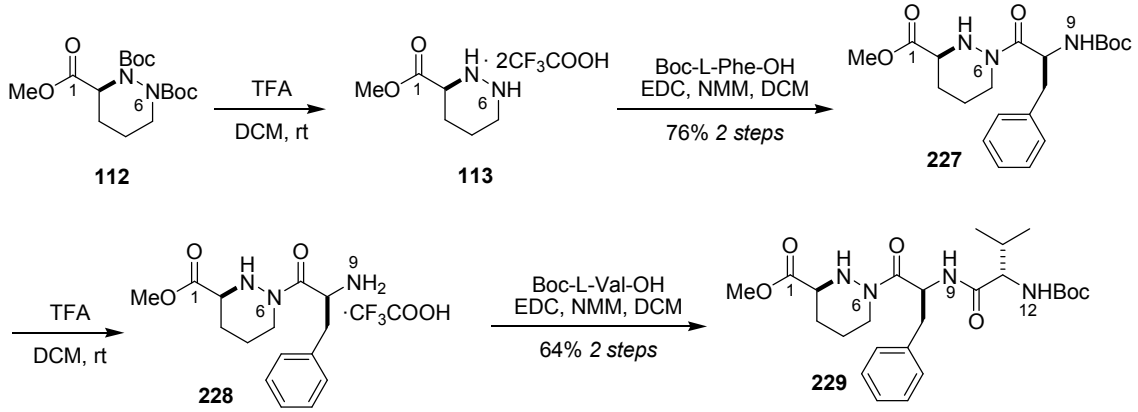
Elaboration of **218** by Dias into the C29-C39 subunit **226** began with acetalization of the diol with *p*-methoxybenzaldehyde dimethyl acetal (**219**) catalyzed by pyridinium *p*-toluenesulfonate. This afforded acetal **220**[72] which was reduced regioselectively with diisobutylaluminum hydride to yield primary alcohol **221** (Scheme 2.29). Swern oxidation of **221** gave aldehyde **222** which was reacted with methyllithium at low temperature to give secondary alcohol **223**. Oxidation of **223** under Swern conditions led to methyl ketone **224** and this was subjected to a boron-mediated aldol rection[73] with aldehyde **225**[74] to furnish *syn* product **226** and thus complete synthesis of the C29-C39 portion of SFA. No further report towards the synthesis of SFA has appeared from the Dias group.



Scheme 2.29 Dias' synthesis of the C29-C39 subunit of SFA (43% yield, *6 steps*)

2.7 Wagner's Synthesis of the C1-C23 Macrolide Analogue of SFA by Ring-Closing Metathesis (2000)

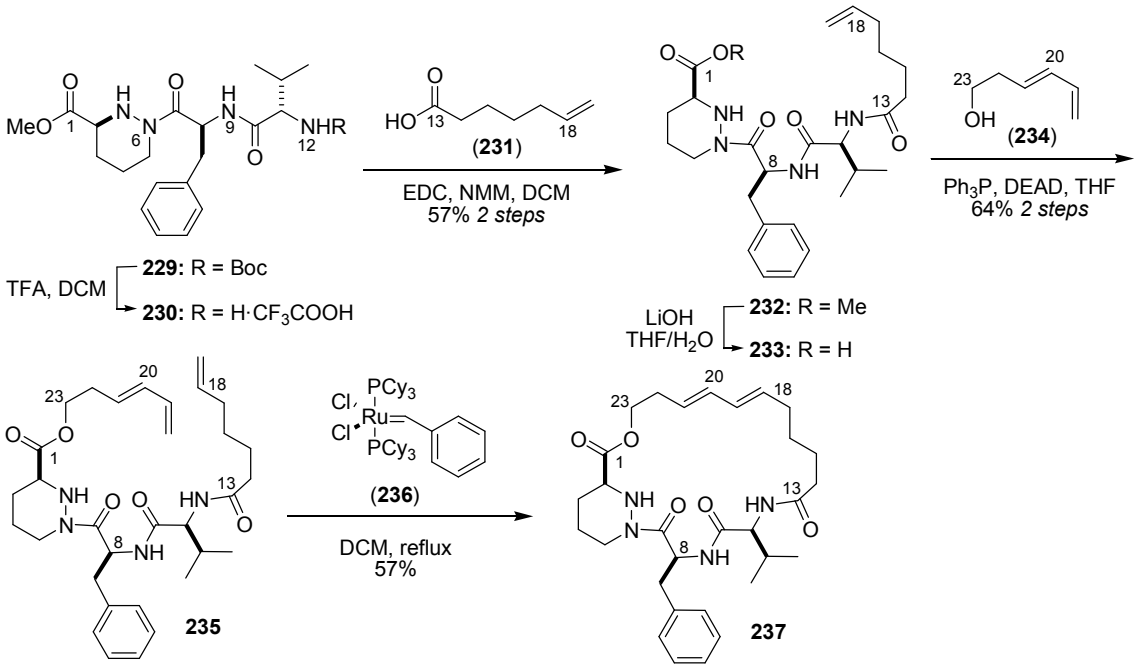
A Novartis group led by Wagner designed a simple macrocyclic analogue of SFA in which the sanglifehrin tripeptide is bridged across its termini by an eleven-carbon dienoic acid to form lactam and lactone connections. The synthesis of this C1-C23 macrolide analogue **237** commenced with construction of C1-N12 tripeptide subunit **229**, as depicted in Scheme 2.30. Thus, the piperazic acid derivative **112** was treated with trifluoroacetic acid to give **113** which was coupled with *N*-*tert*-butoxycarbonyl-L-phenylalanine in the presence of 1-ethyl-3-(3-dimethylamino propyl)carbodiimide and *N*-methylmorpholine to form dipeptide **227**. Treatment of **227** with trifluoroacetic acid furnished amine **228** which was linked to *N*-*tert*-butoxycarbonyl-L-valine using a standard carbodiimide-based coupling procedure to give tripeptide **229**.



112 **113** **227** **228** **229**

Scheme 2.30 Wagner's synthesis of tripeptide **229** (49% yield, *4 steps*)

The key step used to complete the C1-C23 macrocycle **237** was ring-closing metathesis as shown in Scheme 2.31. First, the *N-tert*-butoxycarbonyl group was removed from tripeptide **229** by treatment with trifluoroacetic acid and the resultant amine **230** was acylated with 6-heptenoic acid (**231**) to give amide **232**. Cleavage of the methyl ester from **232** with lithium hydroxide yielded carboxylic acid **233** which was esterified with *E*-3,5-hexadienol (**234**)[75] under Mitsunobu conditions[76] to produce triene **235**. Subjection of the triene to ring-closing metathesis with Grubbs ruthenium(II) carbenoid complex **236**[77] in reflux dichloromethane gave macrocycle **237** in moderate yield. There has been no report from the Novartis laboratory of biological activity associated with this SFA analogue.



Scheme 2.31 Wagner's synthesis of the C1-C23 macrolide analogue of SFA (21% yield, *5 steps*)

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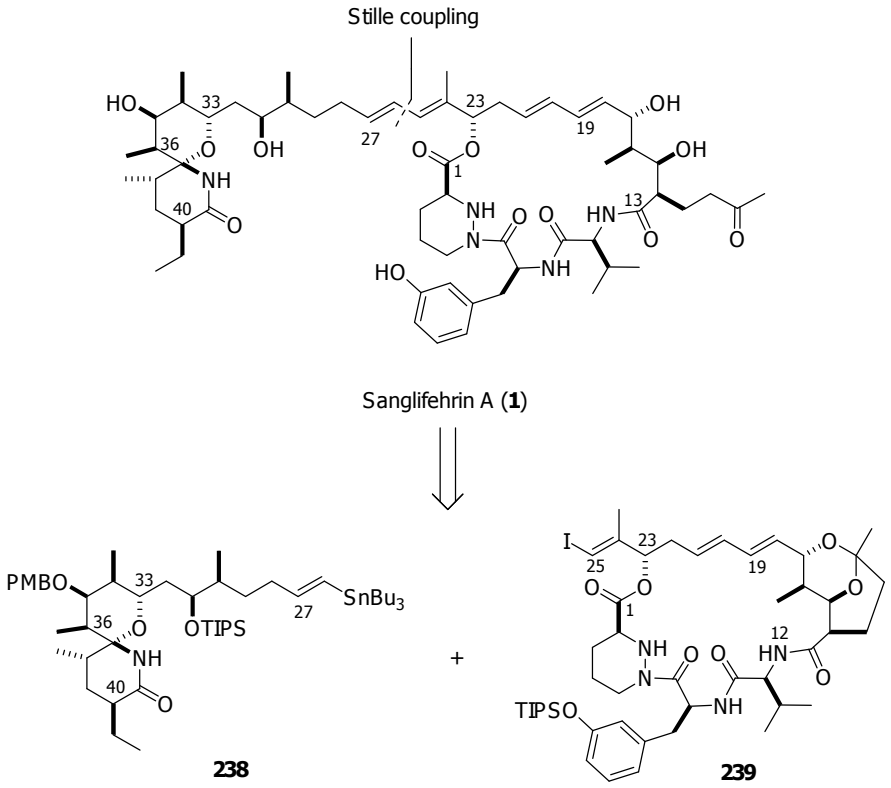
CHAPTER 3: SYNTHESIS OF THE C13-C19 SUBUNIT OF SANGLIFEHRIN A

Featuring a highly substituted [5,5]-spirolactam moiety as well as a 22-membered macrocycle containing a peptidic backbone characterized by unusual *β*–substituted *(S)*-piperazic acid and *(S)*-*m*-hydroxyphenylalanine units, sanglifehrin A (**1**) presents a challenging target from the viewpoint of synthesis. Synthesis of a molecule of this complexity provides an opportunity to develop new strategies and methodologies which can be applied to other complex targets.

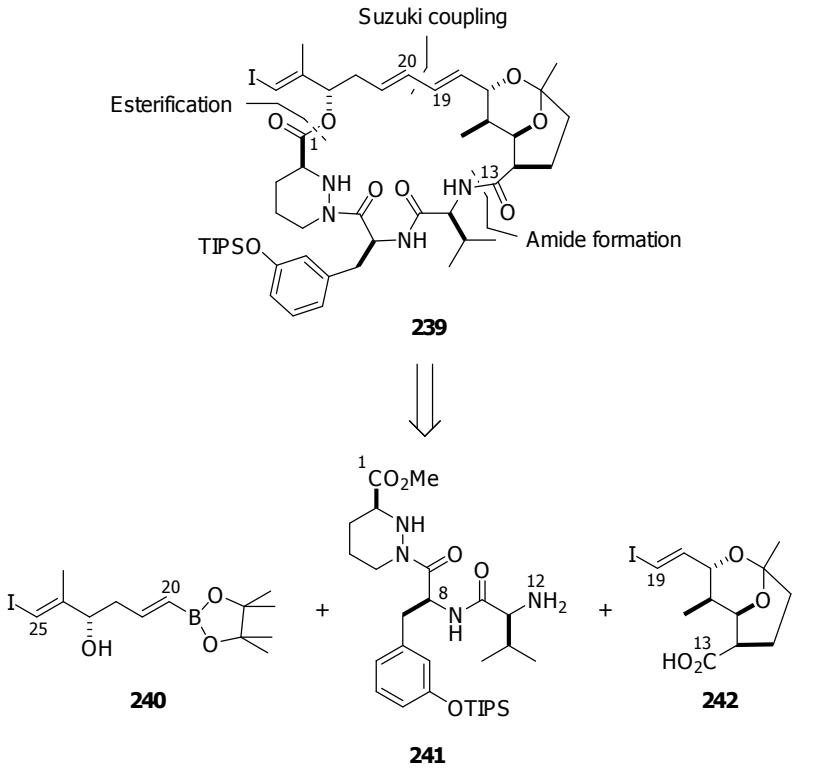
3.1 Retrosynthetic Analysis

Our approach to sanglifehrin A (**1**) relies on the assembly of two principal subunits separated by the C25-C26 bond of the exocyclic *E,E*-diene. This plan leads to a disconnection involving *E*-vinylstannane **238** and *E*-vinyl iodide **239**, assembly of which would use a palladium-mediated Stille coupling[1] as outlined in Scheme 3.1.



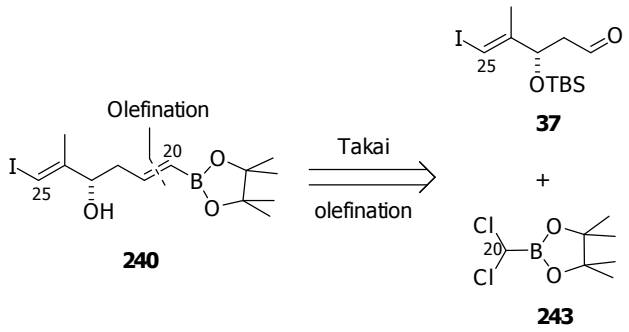
Scheme 3.1 Retrosynthetic analysis of Sanglifehrin A (**1**)

Our approach to the macrocyclic core of **239** involves intramolecular Suzuki coupling[2] with macrocyclization,[3] carbodiimide assisted esterification at C1, and racemization-free amide bond formation between tripeptide **241** and carboxylic acid **242** (Scheme 3.2). Sequential disconnection of the C19-C20, N12-C13, and C1-O bonds reveals alcohol **240**, tripeptide **241**, and carboxylic acid **242** as our key intermediates for assembling macrocycle **239**.



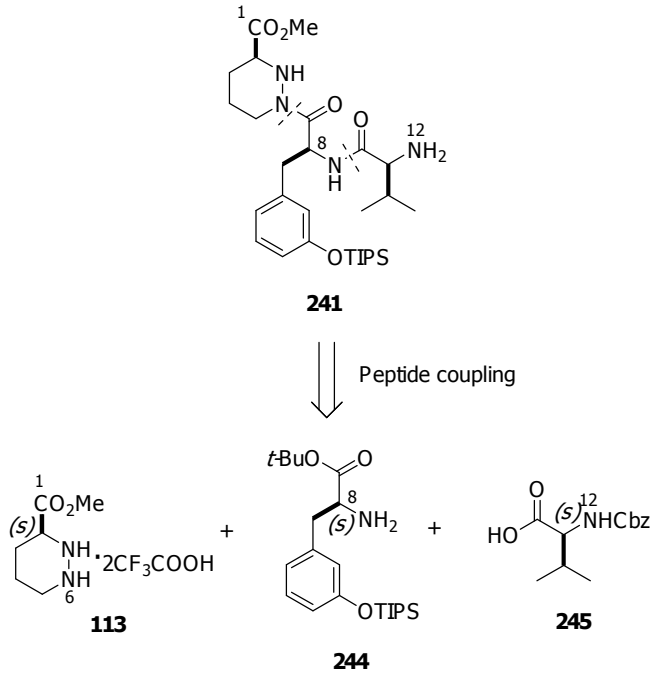
Scheme 3.2 Retrosynthetic analysis of macrocycle **239**

Scheme 3.3 outlines our retrosynthetic analysis of vinyl boronate **240** which would be prepared by Takai olefination[4] of aldehyde **37**[5] with boronate **243**.[6]



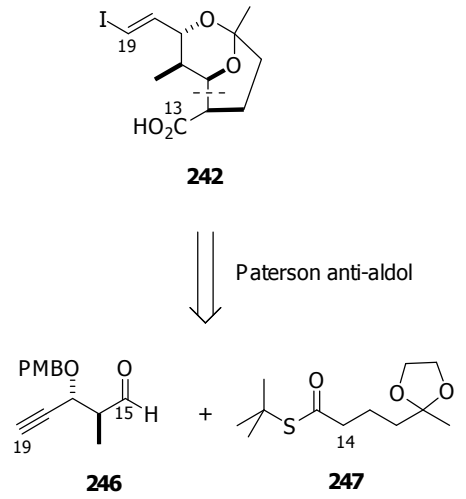
Scheme 3.3 Retrosynthetic analysis of vinyl boronate **240**

In planning the synthesis of tripeptide **241**, *(S)*-piperazic acid methyl ester **113**,[7] *(S)*-*m*-hydroxyphenylalanine derivative **244**, and commercially available *N*-carboxybenzyl-L-valine **245** are required for a properly sequenced peptide coupling. First, we focused our attention on enantioselective synthesis of *(S)*-*m*-hydroxyphenylalanine derivative **244** using a phase-transfer catalytic method,[8] while anticipating that *(S)*-piperazic acid methyl ester **113** would be acquired via a protocol due to Hale[7] (Scheme 3.4).



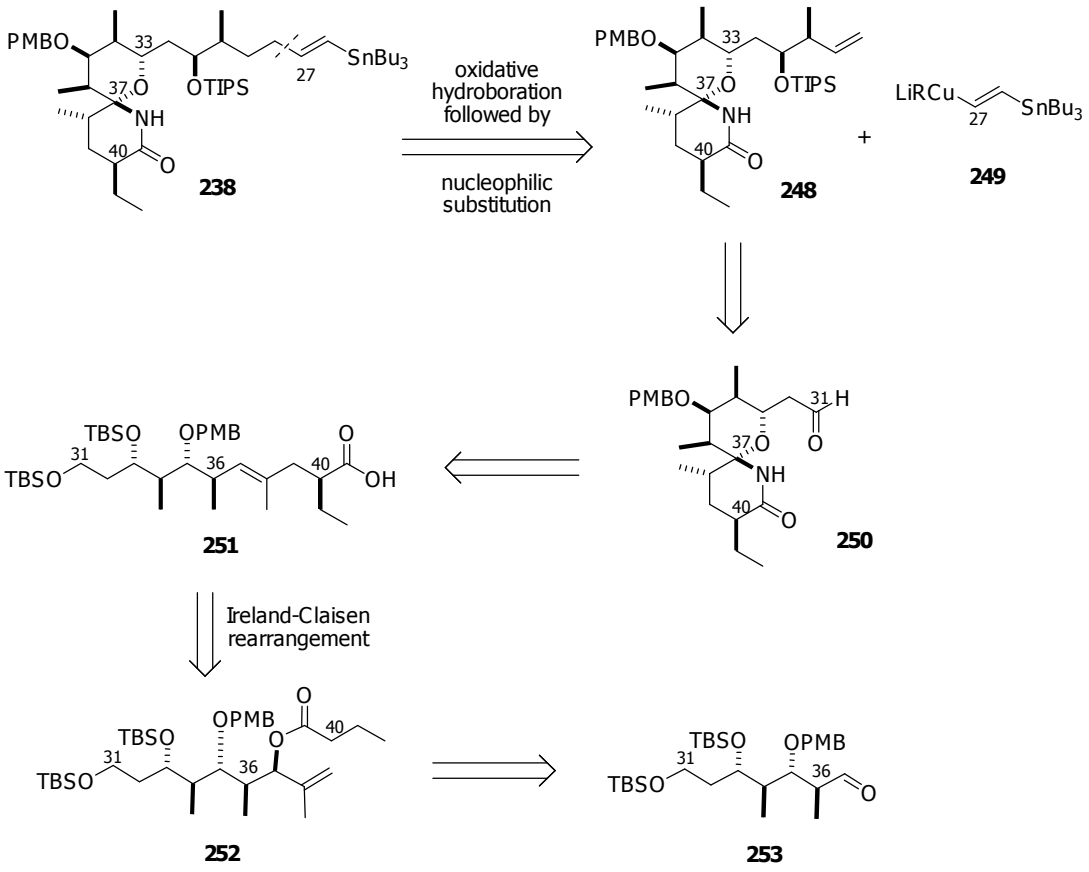
Scheme 3.4 Retrosynthetic analysis of tripeptide **241**

Synthesis of carboxylic acid **242** was initially envisioned from a Paterson anti-aldol reaction[9] of aldehyde **246** and thioester **247**, as illustrated in Scheme 3.5, but this plan subsequently changed to one employing a Masamune anti-aldol coupling.



Scheme 3.5 Retrosynthetic analysis of carboxylic acid **242**

It was envisaged that spirolactam **238** could be constructed through oxidative hydroboration of alkene **248** followed by nucleophilic substitution of the corresponding activated alcohol with organo-copper species **249**[10] (Scheme 3.6). Alkene **248** was anticipated from aldehyde **250** via asymmetric crotylation.[11] The C31-N42 framework in **250** was programmed via cyclization of carboxylic acid **251** which would be generated via an Ireland-Claisen rearrangement[12] of ester **252**. Finally, ester **252** would be obtained in a straightforward sequence from aldehyde **253**.



Scheme 3.6 Retrosynthetic analysis of spirolactam **238**

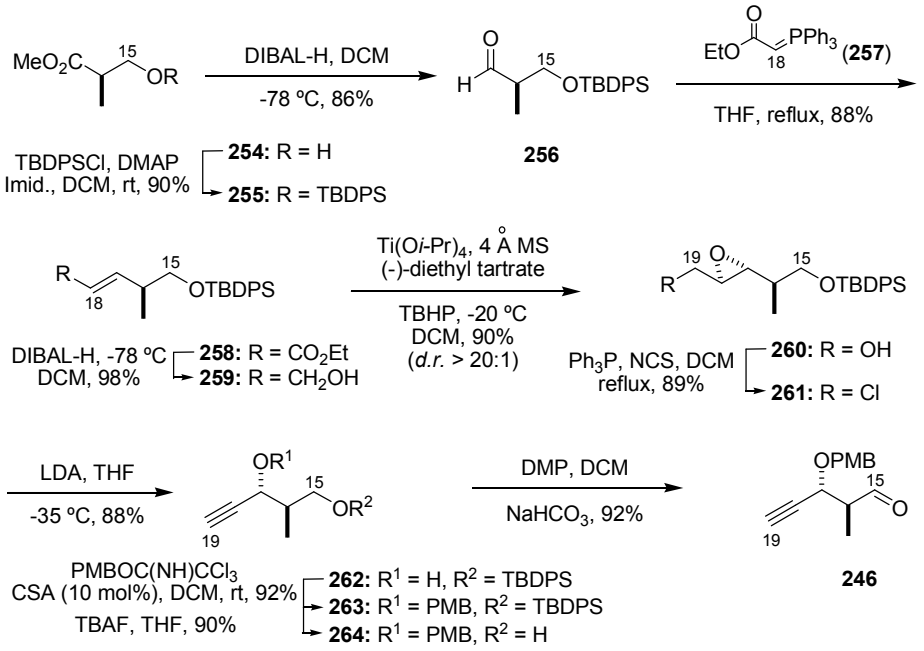
3.2 Synthesis of the C13-C19 Vinyl Iodide 242

3.2.1 First Generation Approach: Construction of the C13-C19 Segment *via* Paterson Anti-Aldol Condensation

Our initial approach to vinyl iodide **242** commenced with the synthesis of known allylic alcohol **259**.[13] As depicted in Scheme 3.7, protection of commercially available *(R)*-methyl 3-hydroxy-2-methylpropanoate (**254**) with *tert*-butyldiphenylsilyl chloride gave silyl ether **255** which was reduced with diisobutylaluminum hydride at

low temperature to aldehyde **256**. Subjection of **256** to olefination with commercially available Wittig reagent **257** in refluxing tetrahydrofuran delivered α,β-unsaturated ester **258** which was reduced with diisobutylaluminum hydride to allylic alcohol **259**. Sharpless asymmetric epoxidation[14] of **259** in the presence of (–)-diethyl tartrate furnished oxirane **260** in high diastereomeric purity, and subsequent conversion of the free hydroxyl group in **260** to chloride **261** was achieved under standard conditions. Based-induced double elimination was employed to convert epoxy chloride **261** to alkyne **262**, as depicted in Figure 3.1. Thus, treatment of **261** with 3.5 equivalents of lithium diisopropylamide generated carbanion **265** which underwent simultaneous epoxide opening to yield alkoxide **266**. Deprotonation of the C18 hydrogen from **266** with a second equivalent of lithium diisopropylamide led to alkenyl anion **267** which expelled chloride ion; aqueous workup then provided alkyne **262**.[15, 16] A *p*-methoxybenzyl group was chosen to mask propargylic alcohol **262** due to its stability and its easy removal with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. Treatment of **262** with *p*-methoxybenzyl bromide under basic conditions at room temperature was investigated first (Table 3.1, entries 1-3) but only recovered starting material was observed. At a higher reaction temperature (40 °C, 12 h, entry 3), **262** was decomposed. Treatment of alcohol **262** with *p*-methoxybenzyl acetimidate under acidic conditions[17] was also investigated (Table 3.1, entries 4-7), and in the presence of 10 mol% pyridinium *p*-toluenesulfonate or 10 mol% camphorsulfonic acid the reaction gave *p*-methoxybenzyl ether **263** in good yield. The primary silyl ether in **263** was unmasked with tetra-*n*-butylammonium fluoride and the resulting alcohol **264** was

oxidized with Dess-Martin periodinane to aldehyde **246** in good overall yield for the nine steps from **254**.



Scheme 3.7 Synthesis of aldehyde **246** (36% yield, 9 steps)

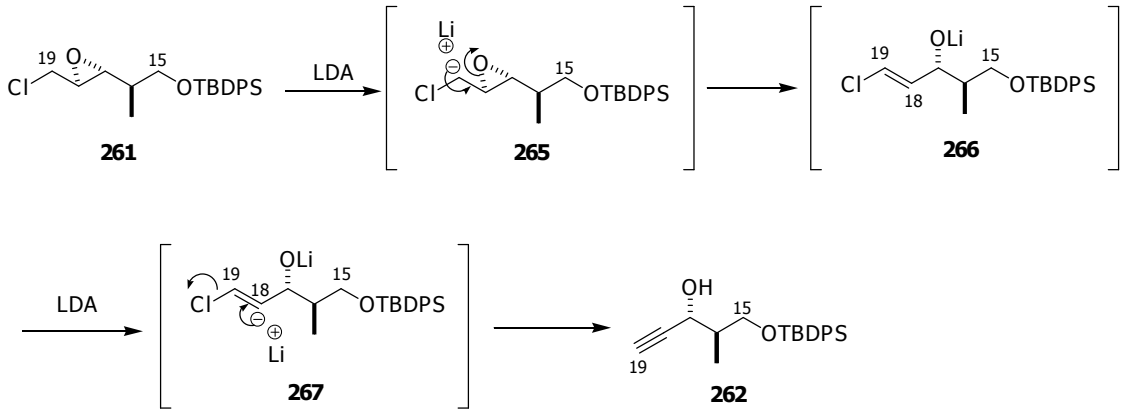
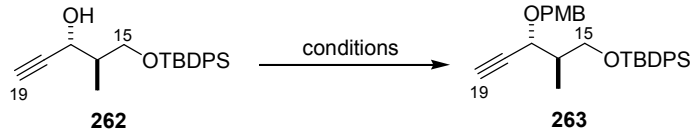


Figure 3.1 Mechanism for base-induced double elimination of **261**

Table 3.1 *p*-Methoxybenzyl protection of alcohol **262** under various conditions

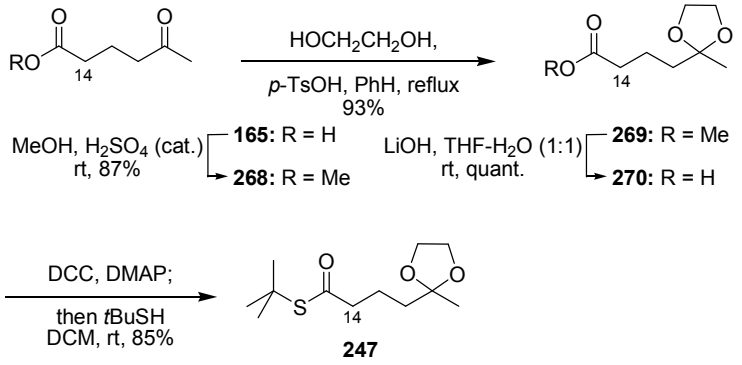


262 **263**

Entry	Conditions	Yield of 263 (%)
1	NaH, PMBCl, TBAI, THF, rt, 3 h	No reaction
2	NaH, PMBCl, TBAI, THF, rt, 12 h	No reaction
3	NaH, PMBCl, TBAI, THF, 40 °C, 12 h	Decomposition
4	PPTS (10 mol%), PMBOC(NH)CCl_3, DCM, rt	80
5	TfOH (20 mol%), PMBOC(NH)CCl_3, Et_2O, rt	Decomposition
6	TFA (20 mol%), PMBOC(NH)CCl_3, Et_2O, rt	No reaction
7	CSA (10 mol%), PMBOC(NH)CCl_3, DCM, rt	92

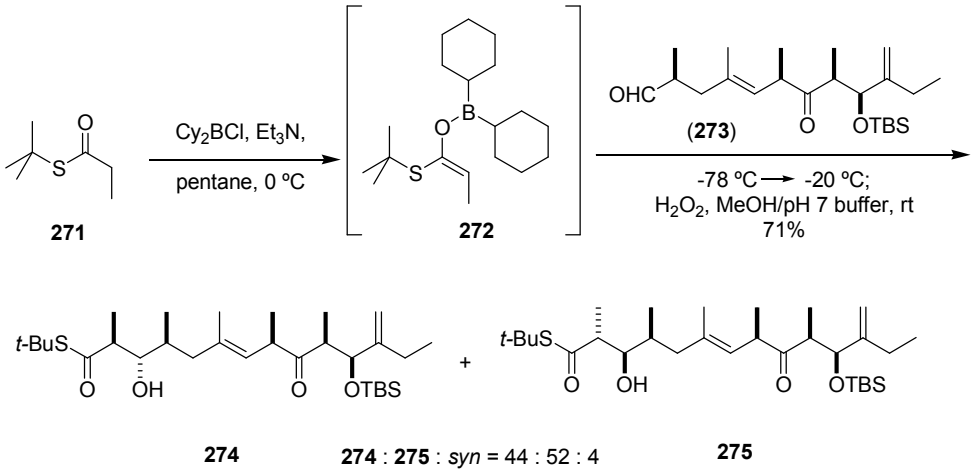
Our next task was preparation of thioester **247** required for its aldol coupling[9] with aldehyde **246**. As shown in Scheme 3.8, thioester **247** was prepared in three steps from commercially available 5-oxohexanoic acid **165**. First, carboxylic acid **165** was transformed into its methyl ester **268**, after which the ketone was reacted with ethylene glycol in the presence of *p*-toluenesulfonic acid to give cyclic ketal **269**. Thioester formation by displacement of methyl esters with *tert*-butyldimethyl aluminum, generated in situ from trimethylaluminum and *tert*-butylthiol in dichloromethane has been reported by Weinreb[18] but treatment of ester **269** with *tert*-butyldimethylaluminum resulted only in decomposition of the starting material. This result, which is probably a consequence of the incompatibility of the ketal function of **269** with strong Lewis acid, forced us to reroute the synthesis of thioester **247** by first

removing the methyl ester from **269** to give carboxylic acid **270**. Treatment of the latter with *N*,*N*-dicyclohexylcarbodiimide in the presence of 4-dimethylaminopyridine followed by addition of *tert*-butyl mercaptan[19] led to thioester **247** in excellent yield.



Scheme 3.8 Synthesis of thioester **247** (69% yield, *4 steps*)

With aldehyde **246** and thioester **247** in hand, in was hoped that stereocontrol through an anti-aldol reaction would lead to the desired configuration at C14 and C15 in carboxylic **242**. In 1995, Paterson and Hulme[9] reported the use of thioester **271** as a substrate for aldol coupling with aldehyde **273** through *(Z)*-dicyclohexylboron enolate **272**. The reaction gave anti-aldol adducts **274**, **275** and a *syn* adduct in a ratio of 44:52:4 and in 71% total yield (Scheme 3.9).



Scheme 3.9 Paterson anti-aldol reaction of propionate thioester **271** with aldehyde **273**

In fact, diastereoselectivity of aldol reactions of α-methyl chiral aldehydes with enol borinates of ethyl ketones has been studied in detail.[20, 21] The dominant element of stereocontrol that determines aldehyde facial selectivity is the minimization of gauche pentane interactions in competing chair-like transition states. In the case of **271**, the low level of intrinsic π-facial selectivity for *Z*-enol borinate **272** addition to aldehyde **273** suggested that both **TS-1** and **TS-2** (where R^2 is methyl) were almost equally favorable (Figure 3.2).

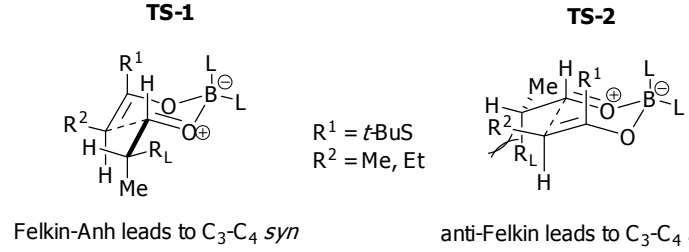
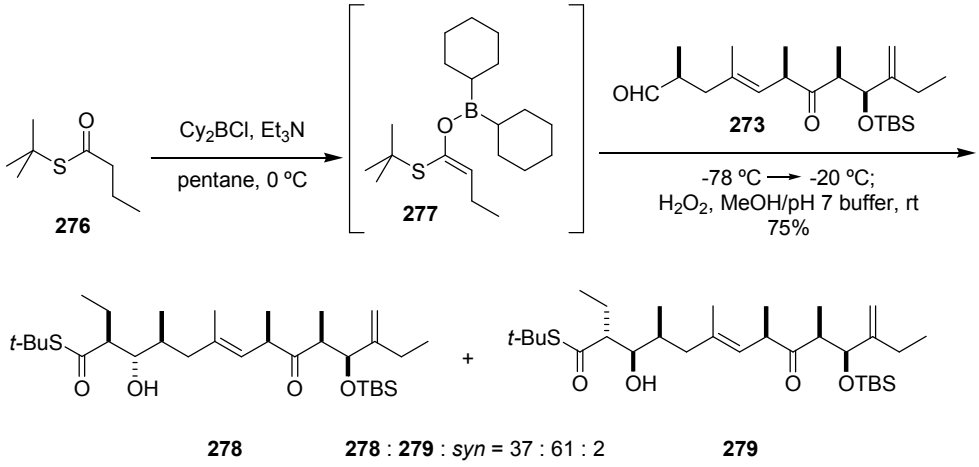


Figure 3.2 Transition states for Paterson anti-aldol reaction

However, when butyrate thioester **276** was used to generate *Z*-enol borinate **277**, the proportion of Felkin addition to **273** was increased over its propionate counterpart **271**, as shown in Scheme 3.10. Anti-aldol products **278** and **279** were now obtained in a ratio of 37:61 (with 2% of a *syn* isomer). The formation of *β*-hydroxy thioester **279** (the Felkin adduct) was favored here due to increased gauche pentane interactions destabilizing **TS-2** relative to **TS-1** (where R^2 is ethyl in Figure 3.2).



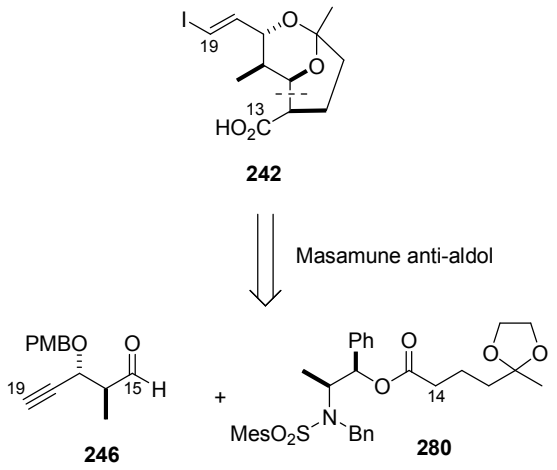
Scheme 3.10 Paterson anti-aldol reaction of butyrate thioester **276** with **273**

We hoped that the enol borinate of our thioester **247**, which has a longer carbon chain than **276**, would exhibit enhanced Felkin selectivity in an anti-aldol reaction with aldehyde **246**, but after many coupling experiments we observed only decomposition of the thioester and no product. We concluded that the ketal in **247** was the culprit and perhaps was unstable in the presence of dicyclohexylboron chloride. In light of this result, as well as a less than optimal prediction of Felkin steroselectivity in

anti-aldol additions of thioester **247**, we decided to change our coupling strategy in favor of one developed by Masamune.[22]

3.2.2 Second Generation Approach: Construction of C13-C19 *via* Masamune Anti-Aldol Condensation

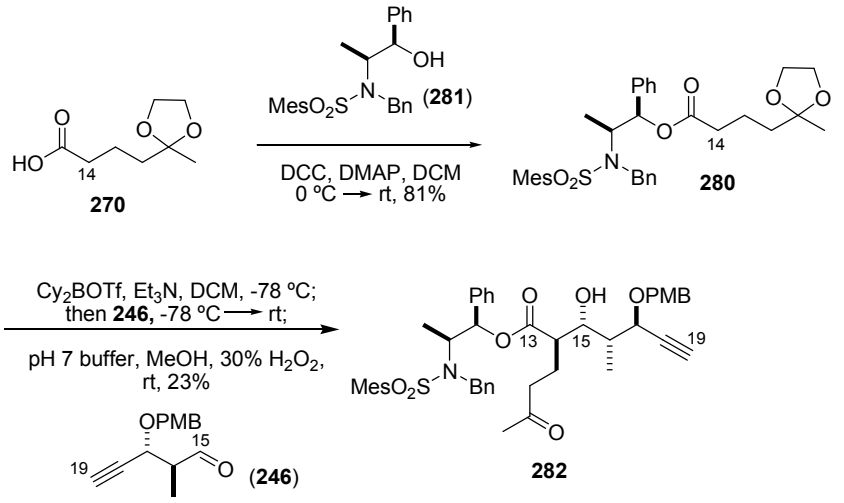
In this plan, we envisioned our carboxylic acid subunit **242** would be prepared by a Masamune anti-aldol reaction of aldehyde **246** with ester **280**, as shown in Scheme 3.11.



Scheme 3.11 Retrosynthetic analysis of carboxylic acid **242** using a Masamune anti-aldol approach

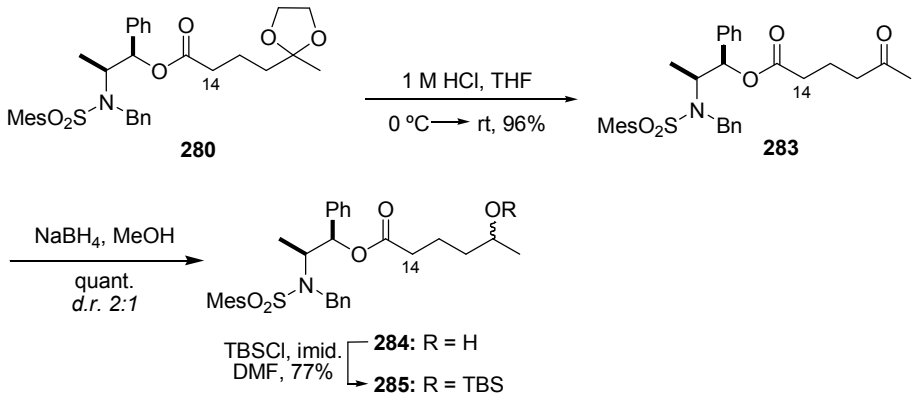
Our second route to carboxylic acid **242** began with the synthesis of ester **281** from carboxylic acid **270** (Scheme 3.12). Ketal acid **270** was esterified with alcohol **281**[22] using *N*,*N*-dicyclohexylcarbodiimide-assisted esterification in the presence of 4-dimethylaminopyridine to afford **280** which was immediately reacted with aldehyde

270 in the presence of freshly prepared dicyclohexylboron triflate. This furnished in low yield the anti-aldol adduct **282** in which the cyclic ketal had been hydrolyzed. Since neither the low yield of this reaction nor loss of ketone protection from the product was compatible with advancement of **282**, a modification was made to **280** which we hoped would circumvent these problems.



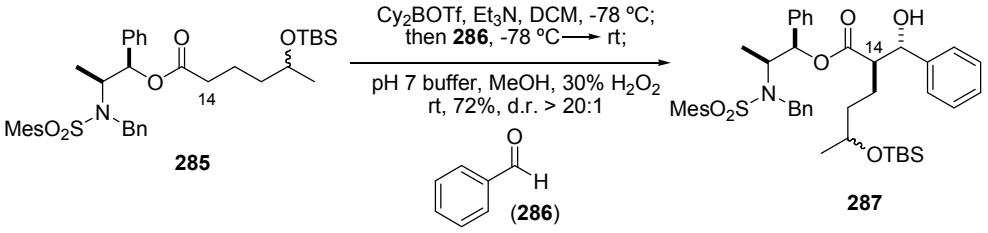
Scheme 3.12 Synthesis of anti-aldol adduct **282** (19% yield, *2 steps*)

To avoid loss of the ketal from **282**, we decided to reduce the keto group of **283** and employ in its place a protected alcohol, as shown in Scheme 3.13. Hydrolysis of cyclic ketal **280** under acidic conditions was achieved in excellent yield and the resultant ketone **283** was reduced with sodium borohydride to afford secondary alcohol **284** in quantitative yield as a mixture of diastereomers (d.r. 2:1 from ^{1}H and ^{13}C NMR). Finally, the free hydroxyl group in **284** was masked as its *tert*-butyldimethylsilyl ether **285**.



Scheme 3.13 Synthesis of ester **285** from cyclic ketal **280** (74% yield, *3 steps*)

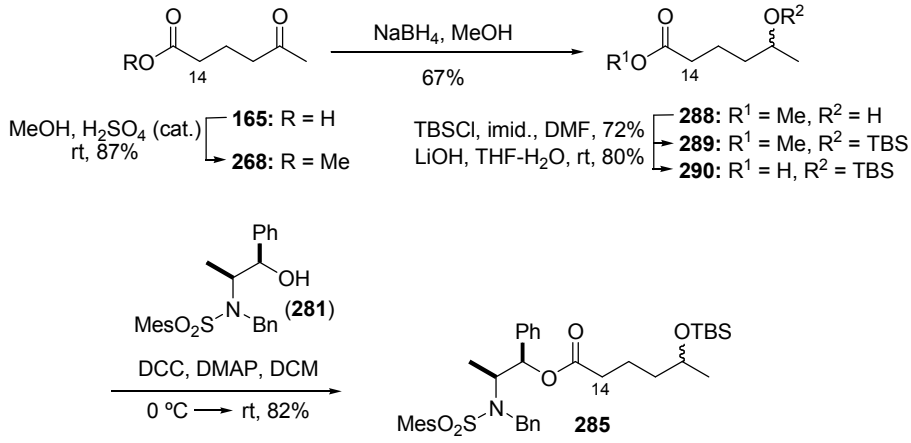
Prior to attempting an aldol coupling of **285** with aldehyde **246**, a model study with benzaldehyde was performed, as shown in Scheme 3.14. Treatment of ester **285** with dicyclohexylboron triflate followed by addition of benzaldehyde (**286**) afforded anti-aldol adduct **287** in good yield. As expected, the *tert*-butyldimethylsilyl ether was retained in this reaction.



Scheme 3.14 Masamune anti-aldol reaction of **285** with benzaldehyde

The synthesis of **287** gave confidence that ester **285** would be a viable candidate for an aldol reaction and we therefore scaled up preparation of **285**. This led to a modified route, as illustrated in Scheme 3.15. For this pathway, commercially available keto acid **165** was treated with methanol in the presence of catalytic sulfuric

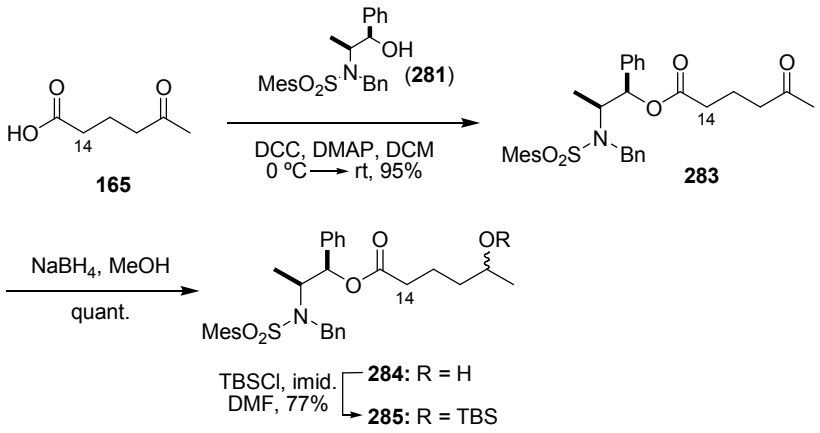
acid and the resulting keto ester **268** was reduced with sodium borohydride to give hydroxy ester **288**. Protection of the hydroxyl group in **288** with *tert*-butyldimethylsilyl chloride in the presence of imidazole gave silyl ether **289**, from which the methyl ester was removed under basic conditions to furnish carboxylic acid **290**. Esterification of **290** with alcohol **281** in the presence of *N*,*N*-dicyclohexylcarbodiimide and 4-dimethylaminopyridine afforded ester **285** in good yield as a mixture of 1:1 diastereomers.



Scheme 3.15 A modified route to ester **285** (28%, *5 steps*)

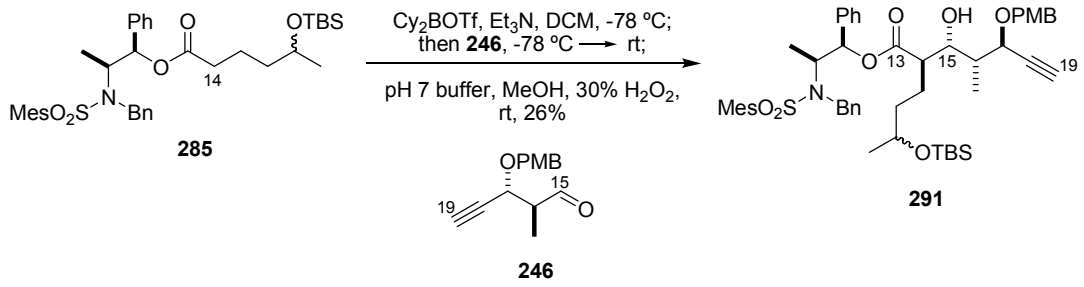
The route from **165** to ester **285** in Scheme 3.15 gave an acceptable overall yield but required two extra steps due to protection and then deprotection of the carboxyl group. If carboxylic acid **165** could be esterified with alcohol **281**, this would reduce the number of steps to **285**, and following this plan we first reacted **165** with alcohol **281** in the presence of *N*,*N*-dicyclohexylcarbodiimide and 4-dimethylaminopyridine to give ketone **283**, as shown in Scheme 3.16. The ketone was reduced with sodium borohydride to secondary alcohol **284** as a mixture of

stereoisomers in quantitative yield (d.r. 2:1). Finally, **284** was reacted with *tert*-butyldimethylsilyl chloride in the presence of imidazole to yield silyl ether **285**.



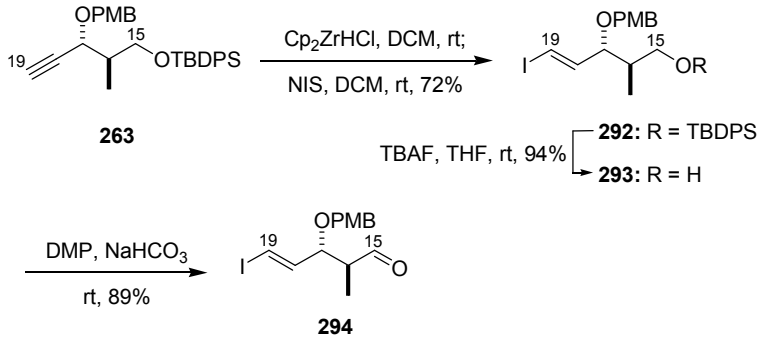
Scheme 3.16 Scaled up route to ester **285** from keto acid **165** (73% yield, *3 steps*)

Having successfully scaled up synthesis of ester **285**, we attempted an aldol reaction with aldehyde **246** under conditions used previously with benzaldehyde (**287**). Unfortunately, this gave an unacceptably low yield of anti-aldol product **291** (Scheme 3.17). This disappointing result caused us to consider whether alkynal **246** was an appropriate substrate for an aldol reaction with **285**, since in practical terms an aldehyde similar to **37** would afford more direct access to our target **242**. A new aldol coupling was therefore designed along this line.



Scheme 3.17 Anti-aldol reaction of aldehyde **246** with ester **285**

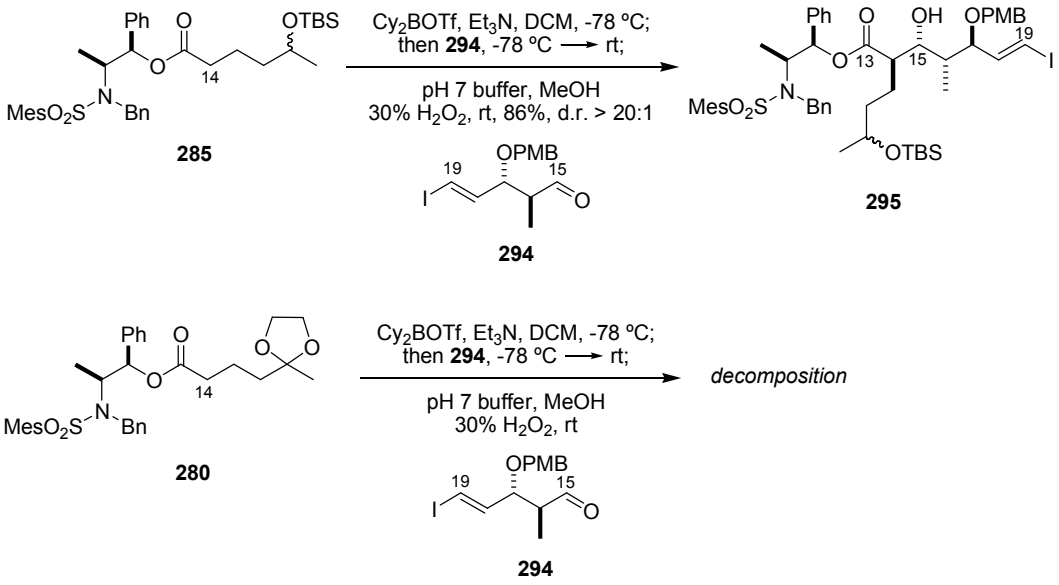
The new aldehyde coupling partner for reaction with ester **285** was iodo alkene **294** which was prepared from **263** in three steps, as shown in Scheme 3.18. Hydrozirconation-iodination of alkyne **263** with bis(cyclopentadienyl)zirconium chloride hydride[23] led to vinyl iodide **292**, which underwent desilylation to primary alcohol **293**. Dess-Martin oxidation of **293** in the presence of sodium hydrogen carbonate delivered aldehyde **294**.



Scheme 3.18 Synthesis of aldehyde **294** from alkyne **263** (60% yield, *3 steps*)

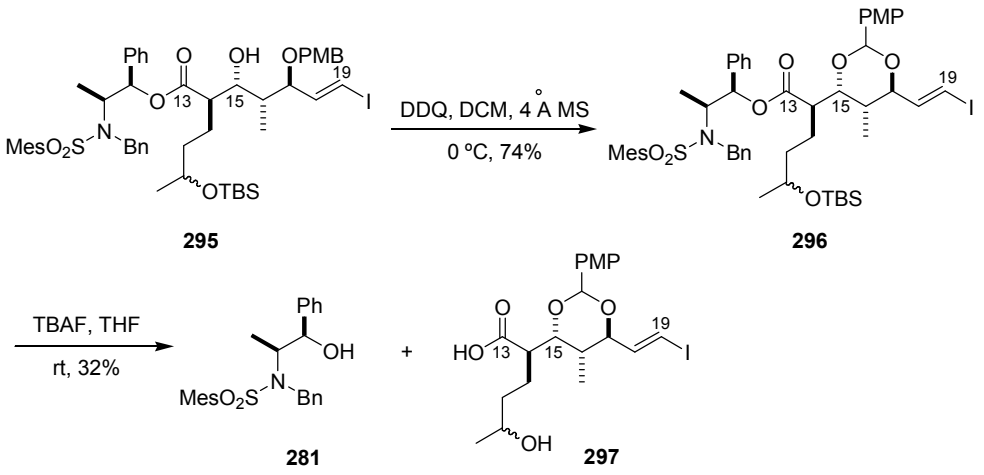
To our delight, subjection of aldehyde **294** to an aldol reaction with **285** under conditions used with benzaldehyde furnished alcohol **295** in excellent yield (Scheme 3.19). In contrast, ester **280** gave no product with **294** and was largely decomposed

under the same conditions, confirming our previous assumption that the cyclic ketal of **280** was incompatible with this reaction.



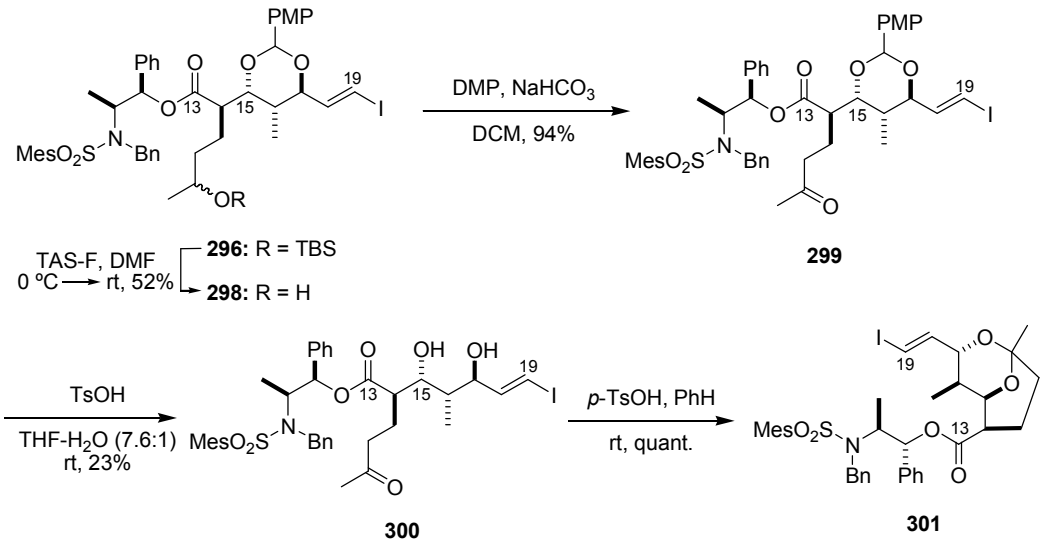
Scheme 3.19 Synthesis of anti-aldol product **295** from **294**

The sulfonamido ester of **295** was retained as a temporary protecting group for the carboxylic acid so that the *p*-methoxybenzyl ether could be reacted with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to provide cyclic acetal **296**.[24] However, when **296** was exposed to tetra-*n*-butylammonium fluoride we not only observed cleavage of the *tert*-butyldimethylsilyl ether but scission of the ester as well. This led to carboxylic acid **297** (32% yield) along with alcohol **281** (Scheme 3.20).

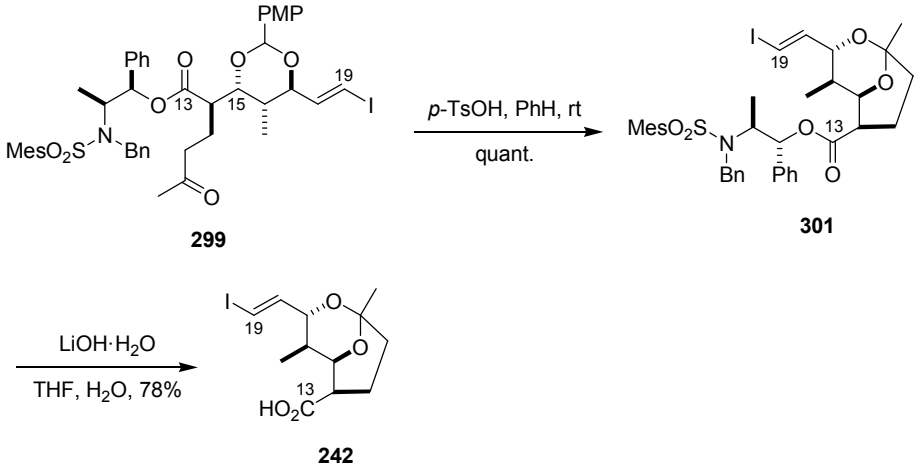


Scheme 3.20 Conversion of **295** to acetal **296** and cleavage to hydroxyl acid **297**

In order to prevent cleavage of the ester while unmasking the silyl ether, **296** was treated with the milder fluoride source tris(dimethylamino)sulfonium difluorotrimethylsilicate (TAS-F). This gave secondary alcohol **298** which was oxidized with Dess-Martin periodinane to ketone **299** (Scheme 3.21). When **299** was subjected to *p*-toluenesulfonic acid in tetrahydrofuran-water, the major product was dihydroxy ketone **300** resulting solely from hydrolysis of the benzylidene acetal; however, internal ketalization of **299** was readily accomplished with the same acid under anhydrous conditions to give cyclic ketal **301** in excellent yield (Scheme 3.22). Having served its dual purpose as a stereocontrolling and a protecting device, the chiral auxiliary was removed from **301** under basic conditions to give carboxylic acid **242**.



Scheme 3.21 Synthesis of cyclic ketal **301** (11% yield, *4 steps*)



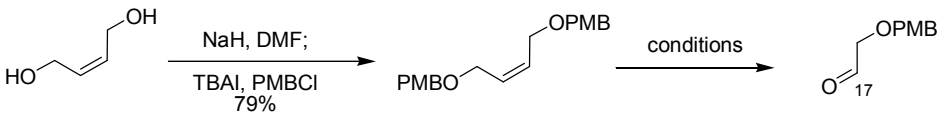
Scheme 3.22 Synthesis of carboxylic acid **242** (78% yield, *2 steps*)

Although this second generation route to **242** was successful in providing useful amounts of material in a linear sequence of 17 steps that gave a 6% overall yield from (*R*)-methyl 3-hydroxy-2-methylpropanoate (**254**), a more efficient pathway

to **242** with fewer steps was deemed desirable. This led to a search for an improved synthesis of **242** which resulted in a third generation route.

3.2.3 Third Generation Approach: Improved Route to 242

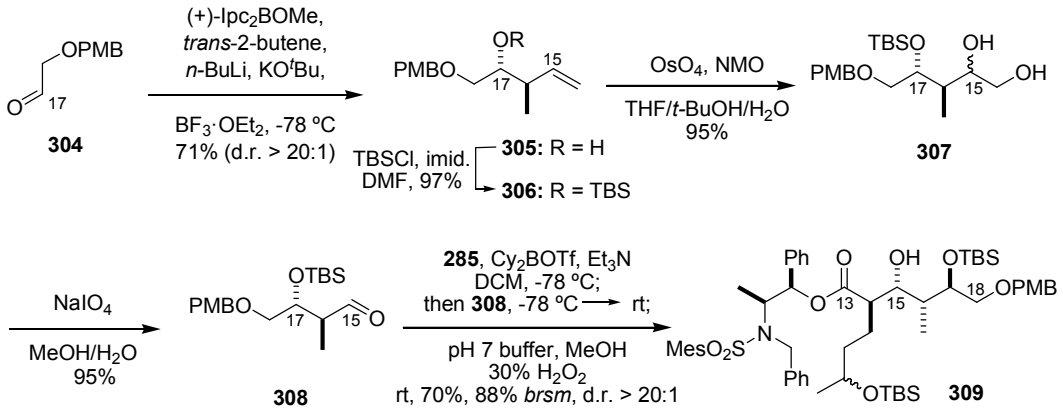
A third route to carboxylic acid **242** was investigated that began with full protection of *cis*-butene-1,4-diol **302** with *p*-methoxybenzyl bromide in the presence of tetra-*n*-butylammonium iodide to give **303** (Scheme 3.23).[25] Oxidative cleavage of olefin **303** was conducted under various conditions as shown in Table 3.2. Although each experiment gave a comparable yield of **304**, we chose ozonolysis for our purpose (entry 1) due to its inexpensive nature and ease of product work up. After oxidative cleavage of **303**, aldehyde **304**[26] was subjected to asymmetric crotylation[11] with *E*-crotyldiisopinocampheylborane to yield homoallylic alcohol **305** with excellent stereoselectivity (d.r. > 20:1, Scheme 3.24). Protection of the hydroxyl group of **305** as its *tert*-butyldimethylsilyl ether **306**[27] was followed by dihydroxylation of the alkene to produce **307**. Oxidative-cleavage of the latter gave aldehyde **308**, after which aldol reaction[22] with ester **285** furnished alcohol **309** in good yield.



Scheme 3.23 Synthesis of aldehyde **304** from diol **302**

Table 3.2 Oxidative cleavage of olefin **303** to aldehyde **304**

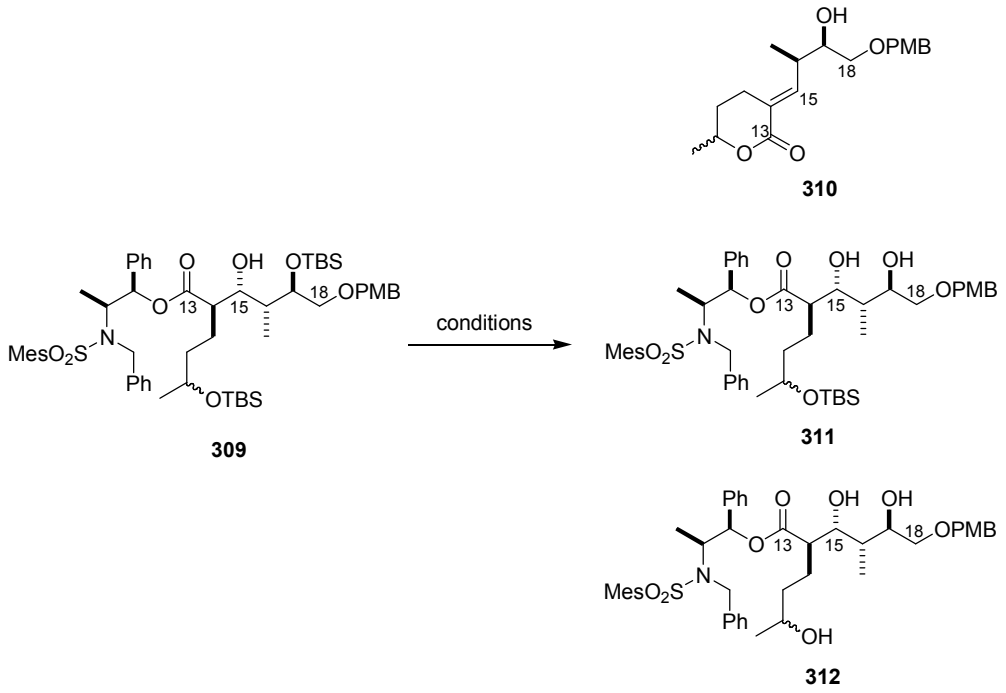
Entry	Conditions	Yield of 304 (%)
1	O_3, DCM, -78 °C; Me_2S, -78 °C to rt	86
2	OsO_4, $NaIO_4$, Et_2O-H_2O (1:1)	88
3	OsO_4, $NaIO_4$, 2,6-lutidine, dioxane-H_2O (3:1)	85



Scheme 3.24 Synthesis of alcohol **309** from **304** (44% yield, *5 steps*)

Our next goal with **309** was deprotection of both *tert*-butyldimethylsilyl ethers without removal of the chiral auxiliary for which the conditions listed in Table 3.4 were explored. After several unsuccessful experiments that led either to *α,β*-unsaturated lactone **310** (entries 1-3) or to mono-desilylated product **311** (entry 4), we found that exposure of **309** to hydrogen fluoride-pyridine complex[28] (entry 5) gave triol **312** in excellent yield.

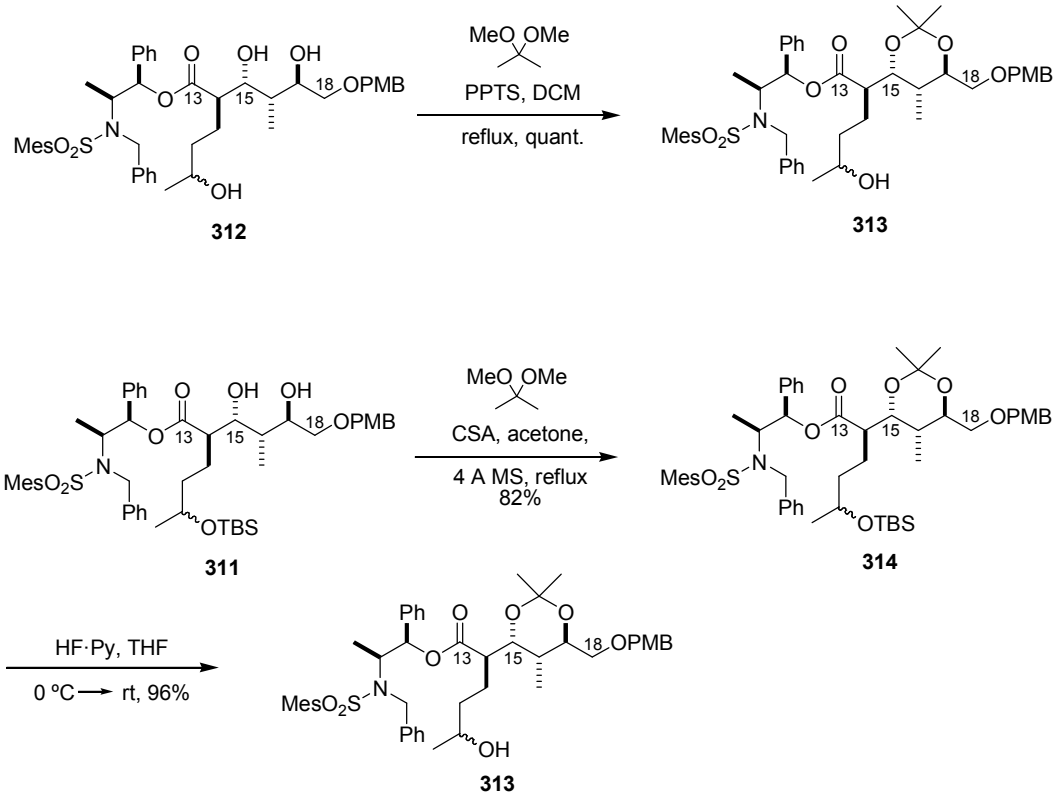
Table 3.3 Deprotection of bis-*tert*-butyldimethylsilyl in **309**



Entry	Conditions	Products	Yield (%)
1	TBAF, THF, rt	**310**	66
2	HF-H_2O, MeCN, rt	**310**	66
3	TAS-F, DMF, 0 °C to rt	**310**	80
4	TAS-F, H_2O, DMF, rt	**311**	84
5	HF·py, THF, 0 °C to rt	**312**	94

With the 1,3-diol moiety of triol **312** now exposed, the latter was reacted with 2,2-dimethoxypropane in the presence of pyridinium *p*-toluenesulfonate to provide acetonide **313**.[29] In a parallel sequence, diol **311** was also converted to its acetonide **314**, which was subjected to desilylation with hydrogen-fluoride pyridine complex to

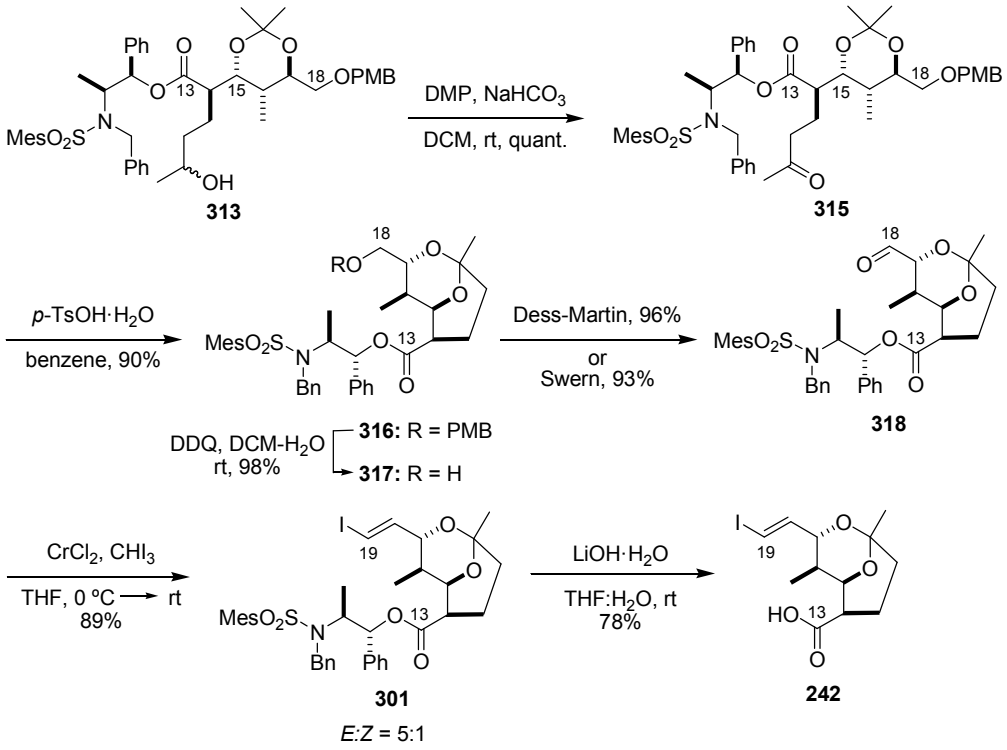
give **313** (Scheme 3.25). In this way, material obtained from **309** by two routes (entries 4 and 5, Table 3.4) were converged at acetonide **313**.



Scheme 3.25 Synthesis of alcohol **313** from triol **312** and diol **311**
(quantitative yield, *1 step from **314***, 79% yield, *2 steps from **313***)

The remaining hydroxyl group in **313** was oxidized with Dess-Martin reagent[30] to ketone **315** which upon exposure to *p*-toluenesulfonic acid underwent internal transketalization to furnish cyclic ketal **316**.[31] The primary hydroxyl group of **316** was unmasked with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[32, 33] and alcohol **317** was oxidized either with Dess-Martin periodinane or under Swern conditions[34] to deliver aldehyde **318**. Takai olefination[35] of **318** in the presence of chromous chloride and

iodoform gave vinyl iodide **301** in good yield (*E*:*Z* 5:1), and final removal of the chiral auxiliary from **301** with lithium hydroxide produced carboxylic acid **242**.



Scheme 3.26 Improved route to **242** (59% yield, *6 steps*)

Whereas our second generation route to vinyl iodide **242** required 17 steps and resulted in 6% overall yield from (*R*)-methyl 3-hydroxy-2-methylpropanoate (**254**), the third generation synthesis gave a better overall yield (13%) and required fewer steps (15). Also, protected primary alcohol in **316** in the third generation route (Scheme 3.26) provides a more flexible locus for connection to its partner than the terminal alkyne in **263** (Scheme 3.18) since alkynes are generally less useful than alcohols in terms of synthetic modification. Lastly, the fact that starting material **302** is

much less expensive than **254** made our third generation route the overwhelming choice for synthesis of **242**.

In summary, synthesis of carboxylic acid **242** demonstrated that a Masamune anti-aldol condensation strategy can be used to set in place the stereochemistry of a complex α-alkyl-β-hydroxy propanoyl function which is not accessible via Paterson's anti-aldol methodology. Considerable effort was devoted to optimizing our route to **242** which was prepared in 15 steps from **302** and with an overall yield of 13%.

3.3 References

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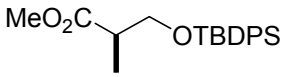
3.4 Experimental Section

General techniques: All reactions requiring anhydrous conditions were conducted in flame dried glass apparatus under an atmosphere of argon. THF, Et_2O, CH_2Cl_2, DMF, benzene and acetonitrile were dried by passage through an activated alumina column under argon. DMSO was distilled from CaH_2 at 15 mm Hg and stored over activated 4Å molecular sieves. Anhydrous MeOH was freshly distilled from calcium hydride. Preparative chromatographic separations were performed on silica gel (35-75 μm); reactions were followed by TLC analysis using silica plates with fluorescent indicator (254 nm) and visualized with a UV lamp or phosphomolybdic acid. All commercially available reagents were purchased from TCI or Aldrich and used as received unless stated otherwise. Melting points were measured on a Büchi melting point apparatus. Optical rotations were measured with a Perkin-Elmer 243 polarimeter at ambient temperature using a 1 mL capacity cell with 1 dm path length. Infrared (IR) spectra were recorded on a Nicolet NEXUS 470 FT-IR using a thin film supported on KBr discs or dispersed in a KBr pellet. ^1H and ^{13}C NMR spectra were recorded in Fourier transform mode at the field strength specified on either a 300 or 400 or 700 MHz spectrometer. Spectra were obtained on $CDCl_3$ solutions on 5 mm diameter tubes, and chemical shifts in ppm (part per million) are quoted relative to the residual signals of chloroform (δH 7.26 ppm, or δC 77.0 ppm). Multiplicities in the ^1H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad;

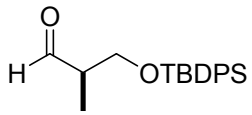
coupling constants (*J*) are reported in Hz. Low (MS) and high (HRMS) resolution mass spectra are reported with ion mass/charge (*m/z*) ratios as values in atomic mass units.



255

(*R*)-Methyl 3-(*tert*-Butyldiphenylsilyloxy)-2-methylpropanoate (255)

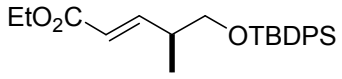
To a stirred solution of (*2R*)-methyl 3-hydroxy-2-methylpropionate (**254**) (2.0 g, 16.9 mmol), imidazole (1.73 g, 25.4 mmol) and DMAP (0.104 g, 0.851 mmol) in dichloromethane (60 mL) at room temperature was added TBDPSCl (5.58 g, 20.3 mmol) and the resulting mixture was stirred for 16 h. The reaction mixture was quenched with water (50 mL) and the organic layer was separated and washed with water and brine, then dried over anhydrous Na_2SO_4. The resulting solution was filtered and concentrated under reduced pressure to give a residue which was purified by flash chromatography (hexanes:EtOAc 60:1) to provide ester **255** as a colorless oil (5.42 g, 90%): $[\alpha]_D^{23}$ -15.5 (*c* 1.00, $CHCl_3$); IR (neat) 3070, 3050, 2932, 2858, 1741, 1472, 1428, 1199, 1176, 1111, 824, 810, 739, 702, 614, 505 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.06 (s, 9H), 1.18 (d, *J* = 6.9 Hz, 3H), 2.74 (m, 1H), 3.71 (s, 3H), 3.74 (dd, *J* = 10.5, 5.7 Hz, 1H), 3.85 (dd, *J* = 10.5, 6.9 Hz, 1H), 7.38-7.45 (m, 6H), 7.66-7.69 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 13.5, 19.2, 26.7, 42.4, 51.5, 65.9, 127.7, 129.7, 133.7, 135.6, 175.0.



256

(*R*)-3-(*tert*-Butyldiphenylsilyloxy)-2-methylpropanal (256)

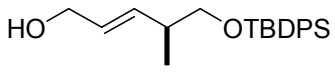
To a stirred solution of ester **255** (788.1 mg, 2.21 mmol) in anhydrous dichloromethane (8.0 mL) at -78 °C was added DIBAL-H (1.0 *M* solution in hexanes, 2.36 mL, 2.36 mmol) dropwise over 8 min. After stirring for an additional 6 h at -78 °C, the reaction mixture was quenched by adding MeOH (0.8 mL) via syringe pump dropwise to maintain the temperature below -70 °C. The resulting mixture was slowly warmed to room temperature and poured into saturated aqueous potassium-sodium tartrate solution (8.0 mL). The mixture was vigorously stirred at room temperature until phase separation occurred (usually 6 h), and the aqueous layer was extracted thoroughly with DCM (3 x 8.0 mL). The combined organic phases were washed with saturated aqueous NaCl (2 x 6.0 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via flash chromatography (5% EtOAc in hexanes) afforded aldehyde **256** (619.5 mg, 86%) as a colorless oil: $[\alpha]_D^{23}$ -20.8 (*c* 0.88, $CHCl_3$); IR (neat) 3071, 3050, 2932, 2858, 2807, 2713, 1738, 1589, 1472, 1428, 1391, 1112, 1035, 824, 741, 702, 614, 505 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.06 (s, 9H), 1.12 (d, *J* = 7.2, 3H), 2.59 (m, 1H), 3.87-3.92 (m, 2H), 7.39-7.47 (m, 6H), 7.65-7.68 (m, 4H), 9.79 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 10.3, 19.2, 26.8, 48.8, 64.1, 127.8, 129.8, 133.2, 135.6, 204.4.



258

(*S*,*E*)-Ethyl 5-(*tert*-Butyldiphenylsilyloxy)-4-methylpent-2-enoate (258)

To a stirred solution of aldehyde **256** (3.37g, 10.3 mmol) in THF (100 mL) was added carbethoxymethylenetriphenyl phosphorane (**257**) (5.39 g, 15.5 mmol) and the resulting mixture was heated at reflux for 16 h. The reaction mixture was cooled to room temperature and quenched with saturated aqueous NH_4Cl (50 mL). The layers were separated and the aqueous phase was extracted with Et_2O (100 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered, and the solvent was removed by rotary evaporation under reduced pressure. The crude product was purified by flash chromatography (10% EtOAc in hexanes) to afford ester **258** (3.61 g, 88%) as a colorless oil: $[\alpha]_D^{25}$ -7.8 (*c* 1.00, $CHCl_3$); IR (neat) 3071, 3050, 2931, 2858, 1722, 1653, 1589, 1472, 1428, 1367, 1390, 1149, 1182, 1087, 1034, 740, 705, 614, 507 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.08 (s, 9H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.32 (t, *J* = 7.2 Hz, 3H), 2.58 (m, 1H), 3.60 (m, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 5.86 (d, *J* = 16.0 Hz, 1H), 6.98 (dd, *J* = 16.0, 7.2 Hz, 1H), 7.39-7.47 (m, 6H), 7.66-7.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 14.3, 15.6, 19.3, 26.8, 39.1, 60.2, 67.5, 121.1, 127.7, 129.7, 133.5, 133.6, 135.6, 151.3, 166.7.

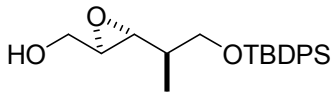


259

(*S*,*E*)-5-(*tert*-Butyldiphenylsilyloxy)-4-methylpent-2-en-1-ol (259)

To a stirred solution of ester **258** (3.50 g, 8.825 mmol) in DCM (90 mL) at -78 °C was added dropwise a solution of DIBAL-H (1*M* solution in hexanes, 35.4 mL, 35.4 mmol). Upon completion of the reaction (about 2 h), as judged by TLC analysis,

the reaction was quenched by pouring the mixture into a vigorously stirred saturated solution of Rochelle's salt (50 mL) and the solution was diluted with Et_2O (50 mL). The phases were separated and the aqueous phase was further extracted with Et_2O (2 x 70 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (10% EtOAc in hexanes) to provide allylic alcohol **259** (3.08 g, 98%) as a colorless oil: $[\alpha]_D^{23}$ -3.6 (*c* 1.00, $CHCl_3$); IR (neat) 3340 (br), 3063, 3050, 2958, 2930, 2857, 1587, 1472, 1467, 1428, 1389, 1112, 1008, 972, 824, 740, 702, 614, 505 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.06 (d, *J* = 7.2 Hz, 3H), 1.08 (s, 9H), 2.44 (m, 1H), 3.56 (m, 2H), 4.09 (m, 2H), 5.64-5.66 (m, 2H), 7.38-7.45 (m, 6H), 7.67-7.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 16.4, 19.3, 26.9, 38.9, 63.9, 68.5, 127.6, 128.8, 129.6, 133.9, 135.5, 135.6.

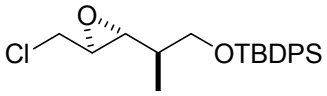


260

((*2R*,*3R*)-3-((*R*)-1-(*tert*-Butyldiphenylsilyloxy)propan-2-yl)oxiran-2-yl)methanol (260)

Ti(O*i*-Pr)$_4$ (30.2 mg, 0.03 mL, 0.106 mmol) was added to a stirred suspension containing 4 Å MS (100 mg) and diethyl (–)-tartrate (26.3 mg, 0.02 mL, 0.128 mmol) in DCM (0.4 mL) at -20 °C under an argon atmosphere. After 15 min, *tert*-butyl hydroperoxide (5.5 *M* in decane, 0.04 mL, 0.213 mmol) was added and the resulting

mixture was stirred for 20 min. A solution of allylic alcohol **259** (37.7 mg, 0.106 mmol) in DCM (0.3 mL) was then added dropwise over 2 min. The mixture was stirred at -20 °C for 36 h and poured into a cold solution of tartaric acid (10% w/w solution in water) saturated with $FeSO_4$ (0.8 mL). Stirring was continued at room temperature for 30 min, and DCM (2.0 mL) was added followed by 30% NaOH (0.1 mL). The mixture was stirred for 30 min and extracted with DCM. The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Flash chromatography (40% EtOAc in hexanes) of the residue furnished epoxy alcohol **260** (35.4 mg, 90%) as a colorless oil: $[\alpha]_D^{25}$ +8.3 (*c* 1.00, $CHCl_3$); IR (neat) 3419 (br), 3071, 3050, 2959, 2930, 2857, 1716, 1653, 1589, 1472, 1428, 1390, 1362, 1113, 1025, 1008, 899 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.03 (d, *J* = 6.8 Hz, 3H), 1.74 (m, 1H), 1.10 (s, 9H), 3.64-3.77 (m, 3H), 3.03 (m, 2H), 3.94 (d, *J* = 12 Hz, 1H), 7.41-7.46 (m, 6H), 7.69-7.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.8, 19.3, 26.9, 37.8, 57.0, 57.5, 61.9, 65.9, 127.7, 129.7, 133.6, 135.6.

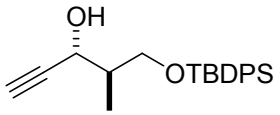


261

***tert*-Butyl((*R*)-2-((*2R*,*3S*)-3-(chloromethyl)oxiran-2-yl)propoxy)diphenylsilane (261)**

To a solution of epoxy alcohol **260** (29.2 mg, 0.0788 mmol) and triphenylphosphine (24.8 mg, 0.0946 mmol) in DCM (5.0 mL) was added *N*-

chlorosuccinimide (12.6 mg, 0.0946 mmol), and the resulting mixture was heated at reflux for 1 h. After cooling to room temperature, the reaction mixture was partitioned between DCM (4.0 mL) and H_2O (5.0 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the residue *via* flash chromatography (1% EtOAC in hexanes) afforded chloride **261** (27.4 mg, 89%) as a colorless oil: $[\alpha]_D^{25}$ +2.5 (*c* 1.00, $CHCl_3$); IR (neat) 3070, 3050, 2960, 2930, 2857, 1472, 1428, 1391, 1263, 1113, 1021, 824, 799, 740, 702, 615, 504 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.03 (d, *J* = 6.9 Hz, 3H), 1.09 (s, 9H), 1.68-1.75 (m, 1H), 2.96 (dd, *J* = 6.9, 1.8 Hz, 1H), 3.10 (dt, *J* = 6.0, 1.8 Hz, 1H), 3.57 (m, 2H), 3.70 (m, 2H), 7.39-7.46 (m, 6H), 7.67-7.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.8, 19.3, 26.9, 37.8, 44.9, 55.9, 60.7, 65.8, 127.7, 129.7, 133.5, 135.6.

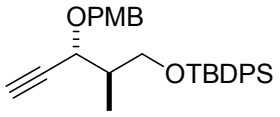


262

(3*R*,4*R*)-5-(*tert*-Butyldiphenylsilyloxy)-4-methylpent-1-yn-3-ol (262)

To neat diisopropylamine (3.30 mL, 23.7 mmol) at 0 °C was added *n*-BuLi (14.2 mL of a 1.52 M solution in hexanes, 21.5 mmol) dropwise. After stirring for 20 min at 0 °C, THF (4.6 mL) was added to provide a 1 M solution of LDA. The LDA (21.5 mL of a 1*M* solution, 21.5 mmol) was added *via* cannula to a solution of chloride **261** (2.38 g, 6.13 mmol) in THF (35 mL) at -35 °C. After 30 min, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl (14 mL), diluted with Et_2O (35

mL) and was washed with H_2O (35 mL), saturated aqueous $CuSO_4$ (35 mL), and brine (35 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the resultant oil *via* flash chromatography (20% EtOAc in hexanes) provided alkyne **262** (1.91 g, 88 %) as a colorless oil: $[\alpha]_D^{23}$ -9.3 (*c* 1.00, $CHCl_3$); IR (neat) 3417 (br), 3308, 3071, 3050, 2959, 2929, 2857, 1712, 1659, 1589, 1471, 1428, 1391, 1362, 1189, 1112, 1028, 999, 823, 802, 740, 702, 614, 505 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.05 (d, *J* = 7.2 Hz, 3H), 1.08 (s, 9H), 2.04 (m, 1H), 2.51 (d, *J* = 2.8 Hz, 1H), 3.35 (d, *J* = 5.6 Hz, 1H), 3.64 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.95 (dd, *J*= 10.4, 4.0 Hz, 1H), 4.55 (br s, 1H), 7.40-7.49 (m, 6H), 7.69-7.72 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.8, 19.2, 26.8, 40.7, 66.4, 67.2, 73.6, 83.8, 127.8, 129.9, 132.9, 135.7.

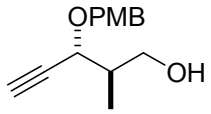


263

((2*R*,3*R*)-3-(4-Methoxybenzyloxy)-2-methylpent-4-ynyloxy)(*tert*-butyl)diphenylsilane (263)

To a stirred solution of alcohol **262** (1.00 g, 2.831 mmol) and freshly prepared 4-methoxybenzyl trichloroacetimidate (3.20 g, 11.322 mmol) in DCM (20 mL) at room temperature was added camphorsulfonic acid (65.8 mg, 0.283 mmol) and the resulting mixture was stirred for 48 h. The reaction mixture was filtered through a pad of Celite, and the pad was washed with 1:2 DCM/hexane (40 mL). The combined

organic layers were washed with saturated aqueous $NaHCO_3$ (25 mL), dried over anhydrous $MgSO_4$, concentrated under reduced pressure and purified by flash chromatography (10% EtOAc/hexanes) to give ether **263** (1.23 g, 92%) as a colorless oil: $[\alpha]_D^{25}$ +28.8 (*c* 1.00, $CHCl_3$); IR (neat) 3287, 3070, 2958, 2930, 2857, 1612, 1513, 1428, 1248, 1112, 1036, 824, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.03 (s, 9H), 1.06 (d, *J* = 6.8 Hz, 3H), 2.11 (m, 1H), 2.46 (d, *J* = 2.0 Hz, 1H), 3.64-3.71 (m, 2H), 3.82 (s, 3H), 4.38 (dd, *J* = 6.4 and 2.0 Hz, 1H), 4.48 (A of ABq, *J* = 11.6 Hz, 1H), 4.78 (B of ABq, *J* = 11.6 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.36-7.46 (m, 6H), 7.64-7.66 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.3, 19.3, 26.8, 40.4, 55.3, 65.0, 69.7, 70.4, 74.9, 81.4, 113.9, 127.6, 129.6, 130.0, 133.6, 133.7, 135.6, 135.7, 159.2; HRMS calcd for $C_{30}H_{36}O_3NaSi$ $[M+Na]^+$ *m/z* 495.2331, found *m/z* 495.2294.

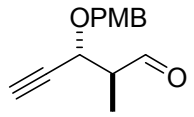


264

(2*R*,3*R*)-3-(4-Methoxybenzyloxy)-2-methylpent-4-yn-1-ol (264)

To a stirred solution of ether **263** (974 mg, 2.06 mmol) in THF (20 mL) at room temperature was added TBAF (2.47 mL of a 1*M* solution in THF, 2.47 mmol). After 14 h, the solution was diluted with Et_2O (80 mL) and was washed with water (60 mL) and brine (60 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the resultant oil via flash chromatography

(10% EtOAc/hexanes) afforded alcohol **264** (433 mg, 90%) as a colorless oil: $[\alpha]_D^{21}$ +123.3 (*c* 1.00, $CHCl_3$); IR (neat) 3427 (br), 3292, 2931, 2867, 1613, 1586, 1514, 1464, 1303, 1247, 1174, 1033, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.03 (d, *J* = 7.2 Hz, 3H), 2.09 (m, 1H), 2.55 (d, *J* = 2.4 Hz, 1H), 3.60 (dd, *J* = 11.2, 7.2 Hz, 1H), 3.72 (dd, *J* = 11.2, 3.6 Hz, 1H), 3.83 (s, 3H), 4.07 (dd, *J* = 7.2, 2.4 Hz, 1H), 4.48 (A of ABq, *J* = 11.2 Hz, 1H), 4.81 (B of ABq, *J* = 11.2 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.3, 40.5, 55.3, 66.1, 70.6, 72.5, 75.1, 81.4, 113.9, 129.3, 129.8, 159.4; HRMS calcd for $C_{14}H_{18}O_3$ $[M]^+$ *m/z* 234.1256, found *m/z* 234.1258.

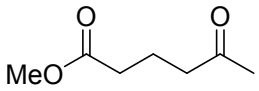


246

(2*S*,3*R*)-3-(4-Methoxybenzyloxy)-2-methylpent-4-ynal (246)

To a stirred mixture of alcohol **264** (25.5 mg, 0.109 mmol) and $NaHCO_3$ (27.4 mg, 0.327 mmol) in DCM (5.0 mL) at room temperature was added Dess-Martin periodinane (69.2 mg, 0.163 mmol) and the mixture was stirred at room temperature for 1.5 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with DCM (3 x 5.0 mL). The combined extract was washed with water (5.0 mL) and brine (5.0 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. Purification of the crude product via flash chromatography (10% EtOAc/hexanes) provided aldehyde **246** (23.2 mg, 92%) as a yellow oil: $[\alpha]_D^{22}$ +133.8 (*c* 1.00, $CHCl_3$);

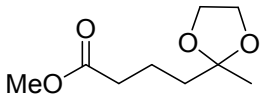
IR(neat) 3280, 2921, 2850, 2720, 2113, 1733, 1613, 1515, 1457, 1248, 1174, 1033, 818, 708, 517 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (d, *J* = 7.2 Hz, 3H), 2.61 (d, *J* = 1.6 Hz, 1H), 2.76 (m, 1H), 3.83 (s, 3H), 4.32 (dd, *J* = 6.4, 1.6 Hz, 1H), 4.49 (A of ABq, *J* =11.2 Hz, 1H), 4.79 (B of ABq, *J* = 11.2 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 9.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 10.5, 50.7, 55.3, 68.3, 70.5, 76.2, 80.2, 113.9, 129.1, 129.8, 159.5, 202.3; HRMS calcd for $C_{14}H_{16}O_3Na$ $[M+Na]^+$ *m/z* 255.0997, found *m/z* 255.0979.



268

Methyl 5-Oxohexanoate (268)

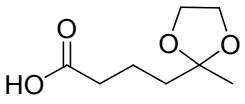
5-Oxohexanoic acid (**165**) (3.01 g, 23.2 mmol) was esterified with MeOH (34 mL) and H_2SO_4 (0.1 mL) at room temperature. After 13 h, most of the methanol was evaporated and the residue was dissolved in ether (50 mL). The solution was rinsed with dilute aqueous $NaHCO_3$ (30 mL), the aqueous layer was extracted with Et_2O (4 x 25 mL) and the combined organic phases were dried over anhydrous $MgSO_4$ and concentrated in *vacuo* to give ester **268** (2.89 g, 87 %) as a pale yellow oil: IR (neat) 2954, 1734, 1716, 1438, 1368, 1157, 1073, 1005, 889, 851 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.91 (m, 2H), 2.15 (s, 3H), 2.36 (t, *J* = 7.2 Hz, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 18.8, 29.9, 33.0, 42.4, 51.6, 173.6, 208.0.



269

Methyl 4-(2-Methyl-1,3-dioxolan-2-yl)butanoate (269)

Methyl ester **268** (2.77 g, 19.2 mmol), ethylene glycol (1.79 g, 28.8 mmol) and *p*-toluenesulfonic acid (25.6 mg, 0.135 mmol) was refluxed for 4 h in benzene (30 mL) beneath a Dean-Stark trap. The solution was rinsed with saturated aqueous $NaHCO_3$ (25 mL) and the aqueous layer was extracted with ether (3 x 25 mL). The combined organic phases were washed with water (25 mL) and saturated aqueous NaCl, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford ketal **269** (3.35 g, 93 %) as a yellow oil: IR (neat) 2982, 2954, 2883, 1743, 1437, 1378, 1259, 1199, 1174, 1135, 1065, 948, 870, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.34 (s, 3H), 1.67-1.80 (m, 4H), 2.26 (t, J = 7.2 Hz, 2H), 3.69 (s, 3H), 3.93-3.97 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 19.6, 23.8, 34.0, 38.3, 51.5, 64.7, 109.7, 174.0.

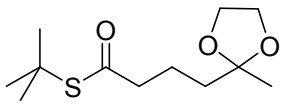


270

4-(2-Methyl-1,3-dioxolan-2-yl)butanoic Acid (270)

To a stirred solution of ester **269** (2.15 g, 9.86 mmol) in THF (30 mL) and water (30 mL) at room temperature was added $LiOH{\cdot}H_2O$ (620 mg, 14.8 mmol) and

the resulting mixture was stirred for 2.5 h. The reaction mixture was acidified to pH 5 with dilute aqueous HCl and extracted with EtOAc (3 x 30 mL). The extract was washed with water (30 mL), brine (30 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to provide crude carboxylic acid **270** (1.83 g, quant.) as a colorless oil: IR (neat) 3300-2900 (br), 2982, 1709, 1379, 1220, 1064, 948, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.32 (s, 3H), 1.77-1.82 (m, 4H), 2.41 (t, J = 6.8 Hz, 2H), 3.93-4.00 (m, 4H), 11.15-11.50 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 19.2, 23.8, 33.9, 38.2, 64.7, 109.7, 179.6; HRMS calcd for $C_8H_{15}O_4$ $[M+1]^+$ *m/z* 175.0970, found *m/z* 175.0974.

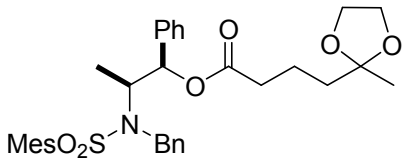


247

***S-tert*-Butyl 4-(2-Methyl-1,3-dioxolan-2-yl)butanethioate (247)**

DCC (1*M* solution in DCM, 1.57 mL, 1.57 mmol) and DMAP 9.6 mg, 0.079 mmol) were added to a solution of carboxylic acid **270** (137 mg. 0.786 mmol) in DCM (4.5 mL) and the resulting mixture was cooled to -5 °C. After stirring for 5 min, *t*-BuSH (89 μL, 0.786 mmol) was added in one portion and stirring was continued at -5 °C for 45 min. The reaction mixture was allowed to warm to room temperature and was kept at that temperature for 14 h, at which point all of carboxylic acid **270** had been consumed. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (10 %

EtOAc/hexanes) to provide thioester **247** (164 mg, 85%) as a yellow oil: IR (neat) 2962, 2880, 1684, 1477, 1457, 1377, 1364, 1251, 1220, 1142, 1065, 968, 947, 872, 616 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.32 (s, 3H), 1.46 (s, 9H), 1.69-1.78 (m, 4H), 2.51 (t, *J* = 1.6 Hz, 2H), 3.91-3.99 (m, 4H); ^{13}C (100 MHz, $CDCl_3$) δ (ppm) 20.2, 23.8, 29.8, 38.1, 44.5, 48.9, 64.7, 109.7, 200.3; HRMS calcd for $C_{12}H_{23}O_3S$ $[M+1]^+$ *m/z* 247.1368, found *m/z* 247.1375.

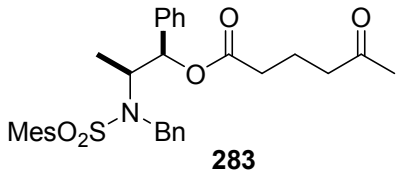


280

(1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl 4-(2-Methyl-1,3-dioxolan-2-yl)butanoate (280)

DCC (1*M* solution in DCM, 3.3 mL, 3.30 mmol) and DMAP (20.1 mg, 0.164 mmol) were added to a stirred solution of carboxylic acid **270** (287 mg. 1.65 mmol) in DCM (5.0 mL) and the resulting mixture was cooled to 0 °C. After stirring for 5 min, alcohol **281** (698 mg, 1.65 mmol) was added in one portion and stirring was continued at 0 °C for 45 min. The reaction mixture was allowed to warm to room temperature and was kept at that temperature for 19.5 h, at which point all of carboxylic acid **270** had been consumed. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography (10 % EtOAc/hexanes) to provide ester **280** (772 mg, 81%) as a white solid: mp 90-92 °C; $[\alpha]_D^{21}$ +14.5 (*c* 1.00, $CHCl_3$); IR(neat) 3063, 3031, 2981,

2940, 2880, 1744, 1604, 1496, 1454, 1379, 1328, 1205, 1149, 1055, 1061, 932, 859, 764, 731, 700, 659, 568, 537 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.15 (d, J = 6.8 Hz, 3H), 1.29 (s, 3H), 1.68-1.57 (m, 4H), 2.27-2.09 (m, 2H), 2.30 (s, 3H), 2.53 (s, 6H), 3.96-3.87 (m, 4H), 4.07 (dq, J = 6.8 and 4.0 Hz, 1H), 4.62 (A of ABq, J_{AB} = 16.8 Hz, 1H), 4.76 (B of ABq, J_{AB} = 16.8 Hz, 1H), 5.85 (d, J = 4.0 Hz, 1H), 6.90 (s, 2H), 6.94-6.92 (m, 2H), 7.37-7.18 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.9, 19.2, 20.9, 23.0, 23.8, 34.0, 38.2, 48.2, 56.7, 64.6, 78.0, 109.7, 126.0, 127.1, 127.4, 127.8, 128.3, 128.4, 132.2, 133.4, 138.6, 138.7, 140.2, 142.5, 171.7; HRMS calcd for $C_{33}H_{42}NO_6S$ $[M+1]^+$ *m/z* 580.2733, found *m/z* 580.2720.



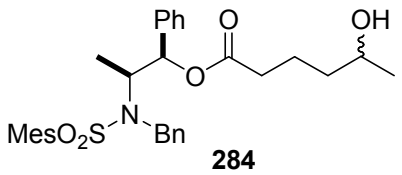
283

(1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl 5-Oxohexanoate (283)

Method A. A solution of ketal **280** (270.8 mg, 0.467 mmol) in THF (8.0 mL) was treated with 1 *M* HCl (1.3 mL) at 0 °C and the resulting mixture was allowed to warm to room temperature. After 38 h, a solution of NaOH (96.0 mg) in water (5.0 mL) was added slowly. The aqueous phase was extracted with Et_2O (10.0 mL) and the combined organic phase was washed with water (2 x 5.0 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by

flash chromatography (30 % EtOAc/hexanes) to provide ketone **283** (240.1 mg, 96%) as a white solid.

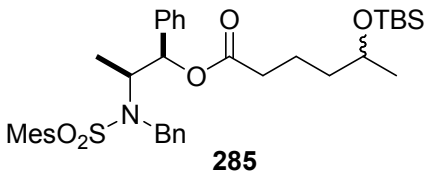
Method B. DCC (1*M* solution in DCM, 10.0 mL, 10 mmol) was added to a stirred solution of DMAP (94.0 mg, 0.768 mmol) and alcohol **281** (3.26 g, 7.68 mmol) in DCM (50 mL) and the resulting mixture was cooled to -5 °C. After stirring for 5 min, carboxylic acid **165** (1.00 g, 7.68 mmol) was added in one portion and stirring was continued at -5 °C for 45 min. The reaction mixture was allowed to warm to room temperature and after 34 h all of carboxylic acid **165** had been consumed. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The crude product was purified by flash chromatography (30 % EtOAc/hexanes) to provide ester **283** (3.91 g, 95%) as a white solid: mp. 105-107 °C; $[\alpha]_D^{25}$ +6.7 (*c* 2.22, $CHCl_3$); IR (neat) 3088, 3064, 3029, 2982, 2940, 1743, 1715, 1604, 1565, 1496, 1454, 1418, 1381, 1322, 1205, 1151, 1073, 1056, 1016, 931, 860, 763, 731, 700, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.14 (d, *J* = 6.8 Hz, 3H), 1.72-1.80 (m, 2H), 2.06-2.14 (m, 1H), 2.09 (s, 3H), 2.19-2.27 (m, 1H), 2.30 (s, 3H), 2.38 (t, *J* =7.2 Hz, 2H), 2.54 (s, 6H), 4.04-4.10 (m, 1H), 4.67 (ABq, *J* = 16.4 Hz, 2H), 5.88 (d, *J* = 4 Hz, 1H), 6.89 (s, 2H), 6.94-6.96 (m, 2H), 7.20-7.35 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 18.5, 20.9, 23.0, 29.9, 32.9, 42.2, 48.1, 56.7, 78.2, 126.0, 127.1, 127.3, 127.9, 128.4, 132.2, 133.3, 138.5, 138.6, 140.2, 142.5, 171.5, 207.9; HRMS (ES) calcd for $C_{31}H_{37}NO_5SNa$ $[M+Na]^+$ *m/z* 558.2290, found *m/z* 558.2288.



284

(1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl 5-Hydroxyhexanoate (284)

To a solution of keto ester **283** (300 mg, 0.560 mmol) in MeOH (22 mL) was added $NaBH_4$ (21.2 mg, 0.560 mmol) and the suspension was stirred at room temperature for 10 min. The reaction mixture was quenched with saturated aqueous NH_4Cl (11 mL) and the aqueous layer was extracted with Et_2O (3 x 25 mL). The combined organic extracts were dried over anhydrous $NaSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (30% EtOAc/Hexanes) to provide alcohol **284** (301 mg, quant.) as a colorless oil: IR (neat) 3560, 3412, 3064, 3032, 2935, 2857, 1743, 1604, 1496, 1454, 1324, 1152, 1016, 859, 765, 732, 701, 659, 567; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.12 (s, 3H), 1.13 (s, 3H), 1.33-1.40 (m, 2H), 1.50-1.69 (m, 3H), 2.09-2.26 (m, 2H), 2.30 (s, 3H), 2.53 (s, 6H), 3.73 (br s, 1H), 4.06-4.14 (m, 1H), 4.59-4.75 (AB q, 2H), 5.88 (d, J = 4.0 Hz, 1H), 6.89 (s, 2H), 6.94-6.96 (m, 2H), 7.21-7.38 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.9, 20.7, 20.9, 23.0, 23.5, 33.9, 38.4, 48.1, 56.7, 67.5, 78.1, 126.0, 127.4, 127.9, 128.4, 132.2, 133.3, 138.5, 138.6, 140.2, 142.5, 172.0; HRMS (ES) calcd for $C_{31}H_{40}NO_5S$ $[M+H]^+$ *m/z* 538.2627, found *m/z* 538.2623.



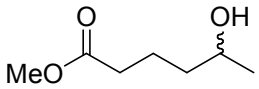
285

(1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl 5-(*tert*-Butyldimethylsilyloxy)hexanoate (285)

Method A. DCC (1*M* solution in DCM, 0.68 mL, 0.68 mmol) was added to a stirred solution of DMAP (4.2 mg, 0.034 mmol) and alcohol **281** (173.2 mg, 0.409 mmol) in DCM (1.7 mL) and the resulting mixture was cooled to -5 °C. After 5 min, carboxylic acid **290** (84.0 mg, 0.341 mmol) was added in one portion and stirring was continued at -5 °C for 45 min. The reaction mixture was allowed to warm to room temperature and after 21 h all of carboxylic acid **290** had been consumed. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The crude product was purified by flash chromatography (10 % EtOAc/hexanes) to provide ester **285** (181.6 mg, 82%) as a colorless oil.

Method B. To a solution of alcohol **284** (275 mg, 0.511 mmol) and imidazole (139 mg, 2.046 mmol) in DMF (5.0 mL) was added TBSCl (154 mg, 1.023 mmol) and the resulting mixture was stirred at room temperature for 24 h. The solution was diluted with Et_2O (10 mL) and was washed with 5% HCl (10 mL), H_2O (5 mL), saturated aqueous $NaHCO_3$ (5 mL) and brine (5 mL), then was dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by flash chromatography (10% EtOAc/Hexanes) to afford TBS ether **285** (256 mg, 77%) as a colorless oil: IR

(neat) 3069, 3032, 2949, 2928, 2856, 1745, 1604, 1496, 1471, 1455, 1379, 1327, 1207, 1155, 1096, 1017, 932, 858, 836, 808, 774, 729, 699, 659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.04, 0.05, and 0.06 (s, 6H), 0.90 and 0.90 (s, 9H), 1.11 (m, 3H), 1.14 and 1.16 (s, 3H), 1.30-1.39 (m, 2H), 1.48-1.53 (m, 1H), 1.57-1.68 (m, 1H), 2.05-2.24 (m, 2H), 2.31 (s, 3H), 2.54 (s, 6H), 3.74-3.78 (m, 1H), 4.05-4.09 (m, 1H), 4.06-4.78 (AB q, 2H), 5.86 (d, J = 3.6 Hz, 1H), 6.90 (s, 2H), 6.93-6.94 (m, 2H), 7.20-7.37 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.7, -4.4, 12.8, 12.9, 18.1, 20.9, 21.2, 23.0, 23.8, 25.9, 34.3, 34.3, 38.9, 39.0, 48.2, 56.7, 68.2, 68.2, 78.0 126.0, 127.1, 127.4, 127.4, 127.8, 128.4, 128.4, 132.2, 133.4, 138.6, 138.7, 138.7, 140.2, 142.5, 171.9; HRMS (ES) calcd for $C_{37}H_{54}NO_5SSi$ $[M+1]^+$ *m/z* 652.3492, found *m/z* 652.3511.

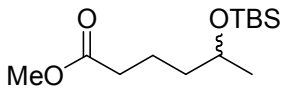


288

Methyl 5-Hydroxyhexanoate (288)

To a stirred solution of ketone **268** (178.9 mg, 1.24 mmol) in MeOH (6.2 mL) was added $NaBH_4$ (51.6 mg, 1.37 mmol) at room temperature and the resulting mixture was stirred for 30 min. The reaction mixture was quenched with water (3.0 mL) and MeOH was removed under reduced pressure. The residue was partitioned between Et_2O (6.0 mL) and water (6.0 mL) and the aqueous phase was extracted with Et_2O (4 x 10 mL). The combined organic phase was washed with brine (10.0 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude

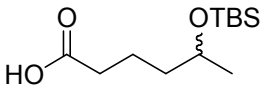
product was purified by flash chromatography (30% EtOAc in hexanes) to furnish alcohol **288** (121.0 mg, 67%) as a colorless oil: IR (neat) 3422 (br), 2963, 2926, 1739, 1437, 1373, 1250, 1201, 1168, 1129, 1018, 986, 943 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (d, *J* = 8.4 Hz, 3H), 1.45-1.52 (m, 2H), 1.65-1.80 (m, 3H), 2.36 (t, *J* = 9.6 Hz, 2H), 3.69 (s, 3H), 3.78-3.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 21.1, 23.5, 33.8, 38.6, 51.6, 67.5, 174.2.



289

Methyl 5-(*tert*-Butyldimethylsilyloxy)hexanoate (289)

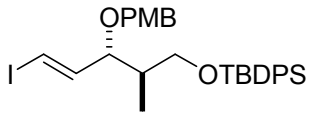
To a stirred solution of alcohol **288** (106.4 mg, 0.73 mmol) and imidazole (198.2 mg, 2.91 mmol) in DMF (7.3 mL) at room temperature was added TBSCl (219.5 mg, 1.46 mmol) and the resulting mixture was stirred for 26 h. The mixture was diluted with Et_2O (8.0 mL) and washed with 5% HCl (8 mL). The aqueous phase was extracted with Et_2O (3 x 8.0 mL) and the combined organic phases were washed with water (15 mL), saturated aqueous $NaHCO_3$ (15 mL) and brine (15 mL). The solution was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography (15% EtOAc in hexanes) to give TBS ether **289** (135.8 mg, 72%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.07 (s, 6H), 0.90 (s, 9H), 1.14 (d, *J* = 6.0 Hz, 3H) 1.41-1.48 (m, 2H), 1.60-1.75 (m, 2H), 2.33 (t, *J* = 7.6 Hz, 2H), 3.69 (s, 3H), 3.80-3.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.8, -4.4, 21.2, 23.7, 25.7, 25.9, 34.1, 39.0, 51.5, 68.2, 174.2.



290

5-(*tert*-Butyldimethylsilyloxy)hexanoic Acid (290)

To a stirred solution of methyl ester **289** (111.0 mg, 0.426 mmol) in THF (1.4 mL) and water (1.4 mL) at room temperature was added $LiOH{\cdot}H_2O$ (26.8 mg, 0.639 mmol). The mixture was stirred for 6 h and was acidified with 1*M* HCl. The aqueous phase was extracted with Et_2O (2 x 2.0 mL) and the organic phase was concentrated under reduced pressure to give carboxylic acid **290** (84.2 mg, 80%) as a colorless oil: IR (neat) 3200-2600, 2957, 2930, 2858, 1712, 1473, 1463, 1414, 1374, 1361, 1255, 1137, 1096, 1042, 1005, 920, 836, 808, 774 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.13 (s, 6H), 0.91 (s, 9H), 1.15 (d, *J* = 6.0 Hz, 3H), 1.45-1.53 (m, 2H), 1.62-1.79 (m, 2H), 2.39 (t, *J* = 7.2 Hz, 2H), 3.81-3.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.8, -4.4, 21.0, 23.7, 25.7, 25.9, 33.9, 38.8, 68.2.

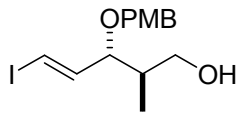


292

((2*R*,3*R*,*E*)-3-(4-Methoxybenzyloxy)-5-iodo-2-methylpent-4-enyloxy)(*tert*-butyl)diphenylsilane (292)

To a solution of alkyne **263** (25.0 mg, 0.0635 mmol) in THF (0.80 mL) was added bis(cyclopentadienyl)zirconium(IV) chloride hydride (65.5 mg, 0.254 mmol)

and the suspension was stirred at room temperature for 30 min. A solution of *N*-iodosuccinimide (57.1 mg, 0.254 mmol) in THF was added dropwise and the dark brown suspension was stirred for 1 h. The resulting mixture was concentrated *in vacuo* to provide a brown solid which was purified by flash chromatography (5% Et_2O/Hexanes) to obtain vinyl iodide **292** (22.9 mg, 72%) as a yellow oil: $[\alpha]_D^{26}$ +16.8 (*c* 1.00, $CHCl_3$); IR (neat) 3070, 2958, 2930, 2857, 1612, 1587, 1513, 1471, 1427, 1389, 1360, 1302, 1248, 1174, 1152, 1112, 1036, 952, 823, 740, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.92 (d, 3H, 6.8 Hz), 1.06 (s, 9H), 1.96 (m, aH), 3.60 (dd, *J* = 6.0, 9.6 Hz, 1H), 3.72 (dd, *J* = 4.8, 9.6 Hz, 1H), 3.82 (s, 3H), 3.90 (t, *J* = 7.6 Hz, 1H), 4.26 (d, *J* = 11.2 Hz, 1H), 4.52 (d, *J* = 11.2, 1H), 6.27 (d, *J* = 14.4 Hz, 1H), 6.49 (dd, *J* = 8.0, 14.4 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.33-7.46 (m ,6H), 7.66 (d, *J* = 7.2 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.6, 19.3, 26.9, 39.9, 55.3, 65.1, 70.4, 78.6, 82.2, 113.8, 114.3, 127.7, 129.2, 129.6, 130.0, 130.3, 133.7, 133.8, 135.6, 145.2, 159.1; HRMS (ES) calcd for $C_{30}H_{37}IO_3NaSi$ $[M+Na]^+$ *m/z* 623.1454, found *m/z* 623.1465.

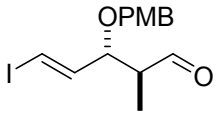


293

(2*R*,3*R*,*E*)-3-(4-Methoxybenzyloxy)-5-iodo-2-methylpent-4-en-1-ol (293)

To a stirred solution of vinyl iodide **292** (13.9 mg, 0.0371 mmol) in THF (0.40 mL) at room temperature was added TBAF (1*M* solution in THF, 50 μL, 0.0446

mmol) and the resulting mixture was stirred for 6 h, then diluted with Et_2O (1.6 mL). The organic phase was washed with H_2O (1.2 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (10% - 30% EtOAc/Hexanes) provided alcohol **293** (7.9 mg, 94%) as a yellow oil: $[\alpha]_D^{25}$ +89.2 (*c* 1.00, $CHCl_3$); IR (neat) 3421, 3039, 2953, 2924, 2844, 1717, 1611, 1586, 1559, 1514, 1464, 1387, 1302, 1248, 1173, 1108, 1062, 1035, 952, 820, 758, 668; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.86 (d, *J* = 6.8 Hz, 3H), 1.84-1.92 (m, 1H), 2.63 (br s, 1H), 3.54-3.69 (m, 3H), 3.83 (s, 3H), 4.29 (d, *J* = 11.6 Hz, 1H), 4.59 (d, *J* 11.6 Hz, 1H), 6.36 (d, *J* = 14.8 Hz, 1H), 6.50 (dd, *J* = 8.0, 14.8 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 13.5, 29.7, 39.5, 55.3, 66.6, 70.5, 79.5, 86.1, 114.0, 129.5, 145.4, 159.4; HRMS (CI) calcd for $C_{14}H_{19}IO_3$ $[M]^+$ *m/z* 362.0379, found *m/z* 362.0371.

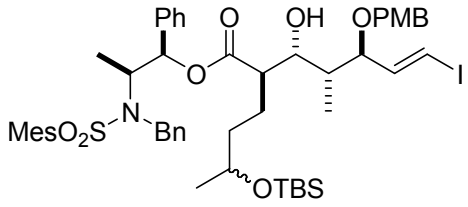


294

(2*S*,3*R*,*E*)-3-(4-Methoxybenzyloxy)-5-iodo-2-methylpent-4-enal (294)

To a stirred suspension of alcohol **293** (128 mg, 0.353 mmol) and $NaHCO_3$ (97 mg, 1.153 mmol) in DCM (8.8 mL) was added DMP (245 mg, 0.577 mmol) and the resulting mixture was stirred for 75 min at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ (8.0 mL) and the aqueous phase was extracted with DCM (3 x 15 mL). The organic phase was washed with H_2O (20 mL),

brine (20 mL), and dried over anhydrous $MgSO_4$. Removal of the solvent provided a crude product which was purified by flash chromatography (10 % EtOAc/hexanes) to obtain aldehyde **294** (113 mg, 89%) as a colorless oil: $[\alpha]_D^{20}$ +90.0 (*c* 1.00, $CHCl_3$); IR (neat) 3036, 2954, 2934, 2862, 2836, 2718, 1727, 1611, 1586, 1514, 1456, 1389, 1340, 1302, 1248, 1175, 1113, 1061, 1035, 953, 820, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.03 (d, *J* = 6.8 Hz, 3H), 2.56-2.64 (m, 1H), 3.83 (s, 3H), 3.96 (t, *J* = 7.6 Hz, 1H), 4.31 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 6.43-6.53 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 9.68 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 10.5, 50.0, 55.3, 70.5, 80.4, 81.7, 114.0, 129.5, 143.9, 159.4, 202.8; HRMS (EI) calcd for $C_{14}H_{17}IO_3$ $[M]^+$ *m/z* 360.0223, found *m/z* 360.0208.



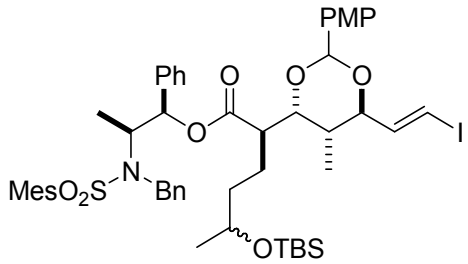
295

(2*R*,3*R*,4*R*,5*R*,*E*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 5-(4-Methoxybenzyloxy)-2-(3-(*tert*-butyldimethylsilyloxy)butyl)-3-hydroxy-7-iodo-4-methylhept-6-enoate (295)

To a solution of ester **285** (199 mg, 0.305 mmol) in DCM (1.4 mL) at room temperature was added triethylamine (0.1 mL, 0.666 mmol) and the resulting mixture was cooled to – 78 °C. A solution of freshly prepared dicyclohexylboron triflate (1*M*

solution in hexane, 0.67 mL, 0.67 mmol) was added dropwise over 2 min. The resulting cloudy mixture was stirred at – 78 °C for 2.5 h, at which point a solution of aldehyde **294** (100 mg, 0.278 mmol) in DCM (1.4 mL) was added dropwise. The reaction mixture was stirred for another 8.5 h at – 78 °C, then was allowed to warm to room temperature over 1 h and was quenched by the addition of pH 7 buffer solution (1.1 mL). The mixture was diluted with MeOH (5.6 mL), and 30% aqueous hydrogen peroxide (0.6 mL) was added carefully. The mixture was stirred vigorously overnight and was concentrated under reduced pressure. The residue was partitioned between water (3.0 mL) and DCM (6.0 mL) and the aqueous layer was extracted with DCM (3 x 6.0 mL). The combined organic extracts were washed with water (6.0 mL), dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated and the residue was purified by flash chromatography (5% EtOAc/hexane) to provide alcohol **295** (242 mg, 86%) as a colorless oil: IR (neat) 3461 (br), 3063, 3025, 2960, 2926, 2853, 1740, 1653, 1607, 1558, 1514, 1497, 1456, 1379, 1323, 1250, 1207, 1153, 1048, 1034, 953, 909, 836, 775, 730, 699, 661; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) -0.02 and -0.00 (s, 6H), 0.85 and 0.86 (s, 9H), 0.89-0.94 (m, 6H), 1.10-1.13 (m, 2H), 1.16-1.20 (m, 3H), 1.21-1.23 (m, 2H), 1.70-1.72 (m, 1H), 2.05 (br s, 1H), 2.33 (s, 3H), 2.40-2.43 (m, 1H), 2.49 (s, 3H), 2.51 (s, 3H), 3.48-3.55 and 3.56-3.62 (m, 1H), 3.69-3.75 (m, 1H), 3.79 and 3.79 (s, 3H), 4.02-4.11 (m, 1H), 4.18-4.23 (m, 1H), 4.26 (A of AB q, J = 11.2 Hz, 1H), 4.57 (B of AB q, J = 11.2 Hz, 1H), 4.59-4.66 (m, 1H), 4.81-4.88 (m ,1H), 5.74-5.78 (m, 1H), 6.37 (dd, J = 3.2, 14.4 Hz, 1H), 6.53 (dd, J = 8.0, 14.4 Hz, 1H), 6.75-6.79 (m, 2H), 6.87 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 6.0 Hz, 2H), 7.12-7.26 (m, 8H),

7.36 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.4, -4.3, 9.6, 13.8, 14.1, 18.0, 20.9, 22.9, 25.8, 36.0 and 36.7, 38.5 and 38.7, 48.2, 49.3 and 49.6, 55.3, 56.7, 68.0 and 68.3, 70.6, 70.9, 77.9 and 78.2, 79.1, 83.7, 114.0, 126.5, 127.0, 127.9, 128.0, 128.1, 128.2, 129.4, 129.5, 132.1, 133.7, 138.4, 139.0 and 139.2, 140.4, 142.4, 145.5, 159.4, 174.5; HRMS (ES) calcd for $C_{51}H_{70}INO_8NaSSi$ $[M+Na]^+$ *m/z* 1034.3534, found *m/z* 1034.3481.

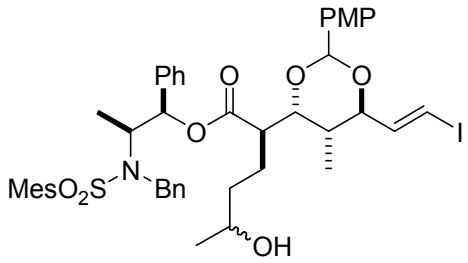


296

(*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 5-(*tert*-Butyldimethylsilyloxy)-2-((4*R*,5*R*,6*R*)-6-((*E*)-2-iodovinyl)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl)hexanoate (296)

To a mixture of alcohol **295** (17.0 mg, 16.8 μmol) and 4 Å MS in DCM (0.4 mL) at 0 °C was added DDQ (6.2 mg, 20.2 μmol) and the resulting mixture was stirred at 0 °C for 2 h. The reaction mixture was warmed to room temperature for 30 min and quenched with saturated aqueous $NaHCO_3$ (0.4 mL). The aqueous layer was extracted with DCM (3 x 0.5 mL) and the organic phase was washed with brine (2.0 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. Flash chromatography of the crude product (10% EtOAc in hexanes) gave acetal **296** (12.6 mg, 74%) as a

colorless oil: IR (neat) 3063, 3031, 2956, 2929, 2855, 1741, 1614, 1516, 1496, 1456, 1382, 1322, 1250, 1205, 1153, 1033, 1010, 910, 834, 775, 731, 698, 660, 566 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) -0.03 and 0.00 (s, 6H), 0.84 and 0.85 (s, 9H), 0.88-0.93 (m, 6H), 1.07-1.28 (m, 5H), 1.98-2.09 (m, 1H), 2.31 (s, 9H), 2.31-2.40 (m, 1H), 2.68-2.79 (m, 1H), 3.45-3.51 and 3.58-3.67 (m, 2H), 3.72-3.80 (m, 1H), 3.83 (s, 3H), 3.90-3.94 (m, 2H), 4.33-4.37 (m, 2H), 4.55-4.59 (m, 1H), 5.63 (d, *J* = 4.8 Hz, 1H), 5.74 (d, *J* = 2.4 Hz, 1H), 6.46-6.51 (m, 1H), 6.60-6.65 (m, 3H), 6.88-6.89 (m, 2H), 7.03-7.07 (m, 2H), 7.13-7.14 (m, 1H), 7.24-7.30 (m, 6H), 7.36-7.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.8 and -4.7, -4.4 and -4.3, 12.7 and 12.7, 14.1 and 14.3, 15.3, 18.0 and 18.1, 20.9, 22.8, 22.9 and 23.1, 23.9, 24.1 and 25.6, 25.8 and 25.9, 36.3, 36.5 and 37.2, 47.0, 47.4, 47.7, 55.3, 56.6, 65.9, 67.7, 68.1, 71.6, 76.7, 77.0, 77.4, 78.2, 78.4, 78.9, 82.2, 98.2, 113.7, 126.5 and 126.6, 127.2, 127.7, 127.8, 128.0, 128.3, 128.4, 131.2, 132.1, 133.2, 138.3, 139.3, 140.5, 142.4, 143.9, 160.0, 173.2 and 173.5; HRMS (ES) calcd for $C_{51}H_{68}INNaO_8SSi$ $[M+Na]^+$ *m/z* 1032.3377, found *m/z* 1032.3325.

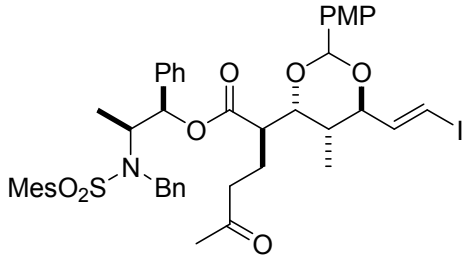


298

(*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 5-Hydroxy-2-((4*R*,5*R*,6*R*)-6-((*E*)-2-iodovinyl)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl)hexanoate (298)

To a solution of TBS ether **296** (9.4 mg, 9.9 μmol) in DMF (0.4 mL) at 0 °C was added TAS-F (6.8 mg, 24.7 μmol) and the resulting mixture was stirred at 0 °C for 1.5 h and then warmed to room temperature. The reaction was monitored by TLC and further quantities (6.8 mg, 24.7 μmol) of TAS-F were added at 8 h and 24 h intervals. After 47 h, the mixture was diluted with EtOAc (1.0 mL) and washed with pH 7 buffer (1.0 mL). The aqueous phase was extracted with EtOAc (3 x 2.0 mL) and the organic extract was dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (40% EtOAc in hexanes) to provide alcohol **298** (4.3 mg, 52%) as a colorless oil: IR (neat) 3522 (br), 3063, 3025, 2960, 2923, 2851, 1738, 1615, 1602, 1518, 1496, 1455, 1402, 1379, 1317, 1250, 1172, 1152, 1118, 1055, 1032, 1010, 991, 910, 861, 831, 774, 731, 699, 660, 597, 566 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.91-1.02 (m, 6H), 1.12-1.61 (m, 6H), 1.75-1.83 (m, 1H), 2.34 (s, 9H), 2.35-2.40 (m, 1H), 2.65-2.78 (m, 1H), 3.45-3.65 (m, 1H), 3.76 (s, 3H), 3.80-3.91 (m, 2H), 4.05-4.35 (m, 4H), 4.45-4.46 (m, 1H), 5.57-5.58 (m, 1H), 5.69 (s, 1H), 6.48-6.52 (m, 1H), 6.58-6.63 (m, 2H), 6.70-6.72 (m, 2H), 6.85-6.95 (m, 4H), 7.00-7.05 (m, 2H), 7.10-7.15 (m, 1H), 7.25-7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.2 and 12.3, 14.3 and 14.3, 20.9, 22.9, 23.4 and 24.1, 23.7 and 23.7, 31.9, 35.6 and 36.2, 47.6 and 48.1, 47.9, 55.4, 56.2 and 56.3, 60.4, 67.0 and 67.6, 78.0,

80.4, 81.4, 96.6 and 96.6, 113.6, 126.8, 126.9, 127.2, 127.7, 128.1, 128.2, 128.6, 128.6, 130.3, 132.1, 133.3, 138.0, 139.1 and 139.3, 140.5, 142.4, 144.3, 160.2, 173.5 and 173.8; HRMS (ES) calcd for $C_{45}H_{54}INO_8SNa$ $[M+Na]^+$ *m/z* 918.2513, found *m/z* 918.2494.

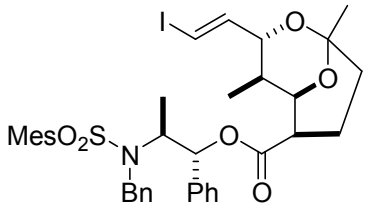


299

(*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 2-((4*R*,5*R*,6*R*)-6-((*E*)-2-Iodovinyl)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl)-5-oxohexanoate (299)

To a stirred mixture of alcohol **298** (17.7 mg, 26.5 μmol) and $NaHCO_3$ (6.7 mg, 79.4 μmol) in DCM (1.3 mL) at room temperature was added DMP (16.8 mg, 39.7 μmol) and the resulting mixture was stirred for 2 h. The mixture was quenched with H_2O (1.0 mL) and the aqueous layer was extracted with DCM (3 x 1.0 mL). The organic phase was washed with brine (2.0 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification of the crude product by flash chromatography (30% EtOAc in hexanes) provided ketone **299** (16.6 mg, 94%) as a colorless oil: $[\alpha]_D^{20}$ +5.8 (*c* 1.00, $CHCl_3$); IR (neat) 3058, 3028, 2824, 2853, 1742, 1718, 1615, 1518, 1496, 1456, 1379, 1320, 1250, 1152, 1120, 1032, 1010, 860, 830, 760, 731, 700, 659 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.89 (d, *J* = 4 Hz, 3H), 1.21-1.32 (m, 3H), 1.69-1.85 (m, 4H), 1.83 (s, 3H), 1.96-2.01 (m, 1H), 2.33 (s, 9H), 2.67-2.71 (m ,1H), 3.76 (s, 3H), 3.91-3.95 (m, 1H), 4.20-4.34 (m, 4H), 4.47 (d, *J* = 4 Hz, 1H), 5.61 (d, *J* = 6.4 Hz, 1H), 5.68 (s, 1H), 6.48-6.52 (m, 1H), 6.64-6.66 (m, 2H), 6.72-6.74 (m, 2H), 6.85-6.89 (m, 4H), 7.04-7.08 (m, 2H), 7.17-7.18 (m, 1H), 7.20-7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.2, 14.4, 20.9, 22.9, 29.7, 31.9, 39.6, 47.1, 47.7, 55.4, 56.0, 77.9, 80.3, 81.3, 96.5, 113.6, 127.0, 127.3, 127.7, 128.2, 128.3, 128.7, 130.2, 130.9, 132.1, 133.1, 138.0, 140.5, 142.5, 144.3, 160.2, 173.5, 207.0; HRMS (ES) calcd for $C_{45}H_{52}INO_8Na$ $[M+Na]^+$ *m/z* 916.2356, found *m/z* 916.2391.



301

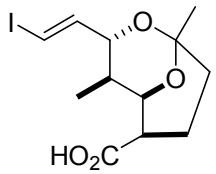
(4*R*,5*R*,6*R*,7*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 7-((*E*)-2-Iodovinyl)-1,6-dimethyl-8,9-dioxa-bicyclo[3.3.1]nonane-4-carboxylate (301)

Method A. To a stirred solution of ketone **299** (5.0 mg, 5.6 μmol) in PhH (0.6 mL) at room temperature was added *p*-TsOH·H_2O (0.1 mg, 0.6 μmol) and the resulting solution was stirred for 8 h. The reaction mixture was diluted with PhH (1.0 mL) and quenched with saturated aqueous $NaHCO_3$ (1.0 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification of the crude

product by flash chromatography (30% EtOAc in hexanes) afforded cyclic ketal **301** (4.6 mg, quant.) as a yellow solid.

Method B. To a stirred suspension of $CrCl_2$ (163 mg, 1.326 mmol) in THF (2.7 mL) at 0 °C was added dropwise a solution of aldehyde **318** (16.8 mg, 0.027 mmol) and CHI_3 (209 mg, 0.530 mmol) in THF (2.7 mL). The ice-bath was removed and the resulting mixture was stirred vigorously at room temperature for 1.5 h. The mixture was diluted with Et_2O (3 mL) and quenched with half-saturated aqueous $Na_2S_2O_3$ (6.0 mL). The aqueous phase was extracted with Et_2O (6.0 mL) and the combined organic phases were washed with H_2O (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Purification of the crude product by flash chromatography (10% EtOAc/hexanes) provided vinyl iodide **301** (18 mg, 89%, *E*:*Z* 5:1) as a yellow oil: $[\alpha]_D^{20}$ +11.2 (*c* 0.50, $CHCl_3$); IR (neat) 3058, 3025, 2924, 2854, 1732, 1604, 1496, 1456, 1381, 1322, 1261, 1204, 1154, 1120, 1075, 1052, 1014, 932, 910, 880, 854, 763, 731, 699, 659 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.43 (d, *J* = 7.7 Hz, 3H), 1.28 (d, *J* = 7.0 Hz, 3H), 1.34 (s, 3H), 1.77-1.83 (m, 1H), 1.93-1.97 (m, 1H), 2.03-2.09 (m, 2H), 2.13-2.20 (m, 1H), 2.30 (s, 3H), 2.42 (s, 6H), 2.82 (dt, *J* = 13.3, 4.2 Hz, 1H), 4.21-4.23 (m, 1H), 4.38 (dd, *J* = 11.2, 6.3 Hz, 1H), 4.41-4.42 (m, 1H), 4.45 (A of AB quartet, *J* = 16.1 Hz, 1H), 4.67 (B of AB quartet, *J* = 16.1 Hz, 1H), 5.79 (d, *J* = 6.3 Hz, 1H), 6.34 (dd, *J* = 14.0, 6.3 Hz, 1H), 6.38 (d, 14.0 Hz, 1H), 6.85 (s, 2H), 6.93 (d, *J* = 7.7 Hz, 2H), 7.17 (t, *J* = 7.7 Hz, 2H), 7.25 (t, *J* = 7.0 Hz, 1H), 7.27-7.29 (m, 5H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) 12.1, 14.9, 20.9, 22.2, 22.9, 29.2, 33.8, 36.5, 43.7, 48.1, 56.4, 71.9, 78.2, 79.6, 80.0, 95.4, 127.0, 127.5, 127.9,

128.2, 128.3, 128.5, 132.1, 132.9, 137.4, 138.0, 140.3, 142.6, 145.7, 170.5; HRMS (ES) calcd for $C_{37}H_{44}INO_6SNa$ $[M+Na]^+$ *m/z* 780.1832, found *m/z* 780.1871.

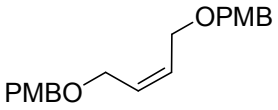


242

(4*R*,5*R*,6*R*,7*R*,*E*)-7-(2-Iodovinyl)-1,6-dimethyl-8,9-dioxa-bicyclo[3.3.1]nonane-4-carboxylic Acid (242)

To a stirred mixture of ester **301** (17.0 mg, 0.022 mmol) in THF (1.5 mL) and H_2O (0.75 mL) at room temperature was added $LiOH{\cdot}H_2O$ (4.7 mg, 0.112 mmol) and the resulting mixture was stirred for 4 days. The reaction mixture was quenched with H_2O (1.0 mL) and acidified with 1*M* HCl until the pH reached 5. The aqueous phase was extracted with EtOAc (2.0 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography (30% EtOAc/hexanes) to give carboxylic acid **242** (6.2 mg, 78%, 83% brsm) as a white solid: $[\alpha]_D^{22}$ +14.1 (*c* 1.00, $CHCl_3$); IR (neat) 3500-2500 (br), 2954, 2923, 2845, 1722, 1604, 1423, 1381, 1114, 956, 792, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.91 (d, *J* = 6.8 Hz, 3H), 1.37 (s, 3H), 1.86-1.89 (m, 1H), 2.06-2.21 (m, 4H), 2.71 (br s, 1H), 4.40 (dd, *J* = 4.0, 10.8 Hz, 1H), 4.48 (d, *J* = 5.6 Hz, 1H), 6.48 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.6, 20.6, 29.5, 30.9, 35.9, 37.7, 72.3, 78.1, 79.9,

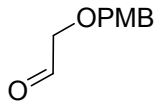
95.9, 145.2, 179.3; HRMS (CI) calcd for $C_{12}H_{17}IO_4$ $[M]^+$ *m/z* 352.0172, found *m/z* 352.0162.



303

(*Z*)-1-((4-(4-Methoxybenzyloxy)but-2-enyloxy)methyl)-4-methoxybenzene (303)

A solution of 2-butene-1,4-diol **302** (3.55 g, 40.28 mmol) in DMF (23 mL) was added to a stirred suspension of NaH (3.71 g, 92.64 mmol from 60% suspension in mineral oil after washing with hexane) in DMF (60 mL). The reaction mixture was then heated to 60 °C and stirred for 2 h. The resulting mixture was treated with TBAI (0.74 g, 2.01 mmol) and PMBCl (12.6 mL, 92.64 mmol) and was stirred at 60 °C for another 2.5 h. After the solution had cooled to room temperature, Et_2O (100 mL) and water (100 mL) were added. The aqueous phase was extracted with Et_2O (3 x 70 mL) and the organic phase was washed with water (2 x 35 mL) and brine (35 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography (hexane/EtOAc 6:1) to afford ether **303** (10.39 g, 79%) as a colorless oil: IR (neat) 2905, 2836, 1612, 1586, 1513, 1464, 1375, 1302, 1248, 1174, 1083, 1034, 819 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.83 (s, 6H), 4.04 (d, *J* = 10.4 Hz, 4H), 4.45 (s, 4H), 5.80 (t, *J* = 4.0 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 4H), 7.28 (d, *J* = 8.4 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$)) δ (ppm) 55.3, 65.5, 71.9, 113.8, 129.4, 129.6, 130.3, 159.2.



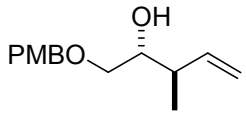
304

2-(4-Methoxybenzyloxy)acetaldehyde (304)

Method A. To a stirred solution of olefin **303** (100 mg, 0.305 mmol) and $NaIO_4$ (144 mg, 0.673 mmol) in Et_2O (0.9 mL) and water (0.9 mL) at room temperature was added a solution of OsO_4 (0.1 *M* solution in *t*-BuOH, 0.06 mL, 6.0 μmol) and the resulting mixture was stirred for 6 h. The solution was diluted with water (5.0 mL) and the aqueous phase was extracted with Et_2O (3 x 5.0 mL). The combined organic extracts were washed with brine (5.0 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography (100% DCM) to provide aldehyde **304** (96.2 mg, 88%) as a brown oil.

Method B. To a stirred solution of olefin **303** (100 mg, 0.305 mmol), $NaIO_4$ (144 mg, 0.673 mmol) and 2,6-lutidine (0.071 mL, 0.609 mmol)) in dioxane (2.25 mL) and water (0.75 mL) at room temperature was added a solution of OsO_4 (0.1*M* solution in *t*-BuOH, 0.06 mL, 6.0 μmol) and the resulting mixture was stirred for 6 h. The mixture was partitioned between water (3.75 mL) and DCM (7.5 mL), and the aqueous phase was extracted with DCM (3 x 5.0 mL). The combined organic extracts were washed with brine (5.0 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography (10% EtOAc in hexanes) to provide aldehyde **304** (93.4 mg, 85%) as a brown oil.

Method C. Ozone was bubbled through a solution of olefin **303** (12.28 g, 37.38 mmol) in DCM (415 mL) and MeOH (13.8 mL) at -78 °C until the solution turned blue. The reaction mixture was stirred until all starting material was consumed as judged by TLC. The ozone source was removed and Ar was bubbled through the solution until it became clear. Me_2S (13.8 mL, 186.89 mmol) was added at -78 °C and the resulting solution was stirred at this temperature for 10 min, before being warmed to room temperature. The solution was stirred for 17 h, water (70 mL) was added, and most of the solvent was removed under reduced pressure. The residue was extracted with Et_2O (4 x 70 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography (40% EtOAc/hexanes) to afford aldehyde **304** (11.54 g, 86%) as a yellow oil: IR (neat) 2998, 2933, 2911, 2867, 2837, 2715, 1735, 1612, 1586, 1514, 1465, 1375, 1303, 1249, 1175, 1109, 1033, 820, 739 cm $^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.82 (s, 3H), 4.08 (s, 2H), 4.58 (s, 2H), 6.91 (s, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 9.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 55.3, 73.3, 75.0, 114.0, 128.9, 129.8, 159.7, 200.6.

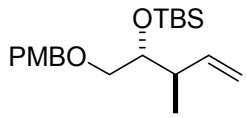


305

(2*R*,3*R*)-1-(4-Methoxybenzyloxy)-3-methylpent-4-en-2-ol (305)

To a stirred suspension of potassium *tert*-butoxide (8.50 g, 69.55 mmol) in dry THF (90 mL) at -78 °C was added trans-2-butene (12.0 mL, 133.74 mmol) followed

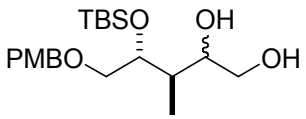
by *n*-butyllithium (1.6*M* in hexanes, 46.8 mL, 74.90 mmol). The resulting yellow solution was stirred at -45 °C for 0.5 h, then was cooled to -78 °C and a solution of (+)-B-methoxydiisopinocampheylborane (22.0 g, 69.55 mmol) in THF (90 mL) was added. The mixture was stirred for 1 h, $BF_3{\cdot}OEt_2$ (9.24 mL, 74.90 mmol) was introduced slowly, and the solution was stirred for 0.5 h. A solution of aldehyde **304** (9.64 g, 53.50 mmol) in THF (90 mL) was added, the mixture was stirred for 4 h and then was quenched at -78 °C with NaOH (3N, 90 mL) followed by a 30% aqueous solution of H_2O_2 (90 mL). The mixture was warmed slowly to room temperature and stirred for 3 h. The aqueous layer was separated and extracted with Et_2O (3 x 250 mL), and the combined organic extracts were washed with brine (250 mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash chromatography (4:1 DCM:Et_2O) to afford alcohol **305** (9.00 g, 71%) as a colorless oil: $[\alpha]_D^{20}$ +5.6 (*c* 3.33, $CHCl_3$); IR (neat) 3465 (br), 3073, 2954, 2906, 2856, 2829, 1612, 1586, 1514, 1464, 1302, 1248, 1174, 1098, 1035, 999, 917, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.06 (d, *J* = 6.8 Hz, 3H), 2.35-2.40 (m, 1H), 2.46 (br s, 1H), 3.41 (dd, *J* = 7.6, 9.6 Hz, 1H), 3.53 (dd, *J* = 3.2, 9.6 Hz, 1H), 3.68 (br s, 1H), 3.83 (s, 3H), 4.50 (s, 2H), 5.08 (s, 1H), 5.12 (d, *J* = 4.0 Hz, 1H), 5.81-5.90 (m, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 16.2, 40.8, 55.3, 72.3, 73.1, 73.5, 113.9, 115.4, 129.4, 130.2, 140.2, 159.3; HRMS (EI) calcd for $C_{14}H_{20}O_3$ $[M]^+$ *m/z* 236.1413, found *m/z* 236.1403.



306

((2*R*,3*R*)-1-(4-Methoxybenzyloxy)-3-methylpent-4-en-2-yloxy)(*tert*-butyl)dimethylsilane (306)

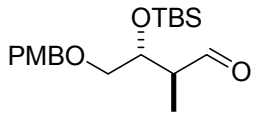
To a stirred solution of alcohol **305** (1.60 g, 6.771 mmol) and imidazole (922 mg, 13.542 mmol) in DMF (13.5 mL) at room temperature was added TBSCl (1.33 g, 8.802 mmol) and the resulting mixture was stirred at room temperature for 18 h. The reaction mixture was quenched with H_2O (15 mL) and extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with water (2 x 20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. Flash chromatography (10% EtOAc in hexanes) of the crude product gave TBS ether **306** (2.29 g, 97%) as a colorless oil: $[\alpha]_D^{20}$ +3.5 (*c* 1.00, $CHCl_3$); IR (neat) 3073, 2956, 2929, 2897, 2857, 1613, 1587, 1514, 1471, 1463, 1361, 1302, 1249, 1173, 1120, 1038, 1005, 914, 836, 776 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.07 (s, 3H), 0.08 (s, 3H), 0.92 (s, 9H), 1.05 (d, *J* = 7.2 Hz, 3H), 2.42-2.45 (m, 1H), 3.33-3.42 (m, 2H), 3.74-3.78 (m, 1H), 3.84 (s, 3H), 4.41-4.48 (AB quartet, 2H), 5.00 (s, 1H), 5.04 (d, *J* = 3.2 Hz, 1H), 5.80-5.88 (m, 1H), 6.90 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.9, -4.2, 17.0, 18.2, 25.9, 41.6, 55.3, 72.9, 73.0, 74.8, 113.7, 114.7, 129.2, 130.6, 140.2, 159.1; HRMS (EI) calcd for $C_{20}H_{34}O_3NaSi$ $[M+Na]^+$ *m/z* 373.2175, found *m/z* 373.2163.



307

(3*R*,4*R*)-5-(4-Methoxybenzyloxy)-4-(*tert*-butyldimethylsilyloxy)-3-methylpentane-1,2-diol (307)

To a stirred solution of olefin **306** (7.00 g, 19.97 mmol) in THF (91 mL), *t*-BuOH (91 mL) and water (18 mL) at 0 °C was added NMO (3.51 g, 29.96 mmol) and the resulting mixture was stirred for 3 min at which point a solution of OsO_4 (0.05 *M* in *t*-BuOH, 20.0 mL, 1.00 mmol) was added. The reaction mixture was stirred for 47 h and quenched with saturated aqueous Na_2SO_3 (55 mL). EtOAc (100 mL) and water (100 mL) were added to the mixture and the aqueous phase was extracted with EtOAc (2 x 200 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. Purification of the crude product by flash chromatography (50% EtOAc in hexanes) gave diol **307** (7.31 g, 95%) as a colorless oil: IR (neat) 3406 (br), 2954, 2929, 2856, 1613, 1587, 1514, 1463, 1361, 1303, 1249, 1173, 1101, 1037, 1005, 953, 836, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.10 (s, 6H), 0.90 (s, 9H), 0.91 (d, *J* = 12.6 Hz, 3H), 1.86-1.93 (m, 1H), 2.40 (br s, 1H), 3.40-3.57 (m, 3H), 3.65-3.72 (m, 3H), 3.83 (s, 3H), 3.96-4.02 (m, 1H), 4.47 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.0, -4.5, 10.9 and 12.6, 18.0 and 18.1, 25.8, 30.3, 37.1 and 39.9, 55.3, 65.0 and 65.4, 71.6 and 72.5, 73.1 and 73.2, 73.8 and 74.0, 113.9, 129.4, 129.7, 159.4; HRMS (CI) calcd for $C_{20}H_{37}O_5Si$ $[M+H]^+$ *m/z* 385.2410, found *m/z* 385.2418.



308

(2*S*,3*R*)-4-(4-Methoxybenzyloxy)-3-(*tert*-butyldimethylsilyloxy)-2-methylbutanal (308)

Method A. A solution of olefin **306** (477.9 mg, 1.363 mmol) in DCM (7.0 mL) and MeOH (7.0 mL) was cooled to -78 °C and a stream of O_3 was bubbled gently through the solution until a light purple color persisted (or TLC showed that all starting material was consumed). The stream of O_3 was terminated and the flask was flushed with Ar until the solution was colorless. $NaBH_4$ (206.3 mg, 5.45 mmol) was added slowly at -78 °C and the mixture was allowed to warm to room temperature. The mixture was concentrated and EtOAc was added (7.0 mL). The organic phase was washed with H_2O (7.0 mL) and the aqueous phase was extracted with EtOAc (3 x 7.0 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated to provide the crude product which was purified by flash chromatography (20% EtOAc in hexanes) to give (2*R*,3*R*)-4-(4-Methoxybenzyloxy)-3-(*tert*-butyldimethylsilyloxy)-2-methylbutan-1-ol (210.7 mg, 44%) as a colorless oil: $[\alpha]_D^{24}$ +9.8 (*c* 2.35, $CHCl_3$); IR (neat) 3450, 2949, 2922, 2857, 1613, 1587, 1515, 1471, 1361, 1302, 1247, 1173, 1085, 1035, 957, 835, 777, 671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 008 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 1.03 (d, *J* = 7.2 Hz, 3H), 1.91 (m, 1H), 2.87 (br s, 1H), 3.45-3.61 (m 3H), 3.72-3.75 (m, 1H), 3.83 (s, 3H), 3.85-3.89 (m, 1H), 4.47 (AB quartet, 2H),

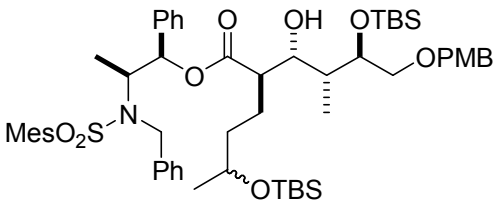
6.90 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.0, -4.3, 14.3, 18.1, 25.9, 37.8, 55.3, 64.8, 72.6, 73.1, 75.8, 113.8, 129.4, 130.0, 159.3; HRMS (ES) calcd for $C_{19}H_{35}O_4Si$ $[M+H]^+$ *m/z* 355.2305, found *m/z* 355.2292. The alcohol was used immediately in the next step.

To a stirred solution of oxalyl chloride (22 μL, 0.257 mmol) in DCM (0.85 mL) at -78 °C was added dropwise a solution of DMSO (31 μL, 0.434 mmol) in DCM (0.85 mL) and the resulting mixture was stirred for 15 min, at which point a solution of the alcohol prepared above (70.0 mg, 0.197 mmol) in DCM (0.50 mL) was added slowly. The cloudy mixture was stirred for 10 min and Et_3N (0.14 mL, 0.987 mmol) was added dropwise. The reaction mixture was stirred for 30 min and warmed to 0 °C. H_2O (1.5 mL) was added and the aqueous phase was extracted with DCM (2 x 2.5 mL). The organic phase was washed with brine (2.5 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude product by flash chromatography (10% EtOAc in hexanes) furnished aldehyde **308** (61.3 mg, 88%) as a yellow oil.

Method B. To a stirred solution of alkene **306** (1.5 g, 4.279 mmol) in dioxane-water (3:1, 44 mL) was added 2,6-lutidine (0.99 mL, 8.558 mmol), OsO_4 (0.05 *M* in 2-methyl-2-propanol, 1.71 mL, 0.0856 mmol), and $NaIO_4$ (3.661 g, 17.115 mmol). The mixture was stirred at room temperature and monitored by TLC. After the reaction was complete (1.5 h), water (55 mL) and DCM (110 mL) were added. The organic layer was separated, and the aqueous layer was extracted with DCM (3 x 55 mL). The

combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed and the crude product was purified by flash chromatography (20% Et_2O/Hexanes) to afford aldehyde **308** (1.140 g, 76%) as a pale yellow oil.

Method C. To a stirred mixture of diol **307** (426.1 mg, 1.11 mmol) in MeOH (7.4 mL) and water (3.7 mL) at 0 °C was added $NaIO_4$ (1.42 g, 6.65 mmol) and the resulting mixture was allowed to warm to room temperature with stirring over 1.5 h. The reaction mixture was partitioned between DCM (13 mL) and water (13 mL) and the aqueous phase was extracted with DCM (20 mL). The organic phase was washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10% EtOAc in hexanes) to deliver aldehyde **308** (372.7 mg, 95%) as a colorless oil: $[\alpha]_D^{20}$ +39.5 (*c* 1.00, $CHCl_3$); IR (neat) 2955, 2931, 2857, 2709, 1725, 1613, 1586, 1514, 1464, 1361, 1302, 1250, 1174, 1103, 1038, 1006, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.08 (s, 3H), 0.09 (s, 3H), 0.90 (s, 9H), 1.12 (d, *J* = 7.0 Hz, 3H), 2.58-2.65 (m, 1H), 3.47-3.49 (m, 2H), 3.83 (s, 3H), 4.11-4.15 (m, 1H), 4.45 (s, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 9.76 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.1, -4.4, 10.0, 18.0, 25.7, 50.0, 55.3, 71.7, 72.7, 73.1, 113.8, 129.3, 130.0, 159.3, 203.8; HRMS (ES) calcd for $C_{19}H_{32}O_4NaSi$ *m/z* 375.1968, found *m/z* 375.1976.

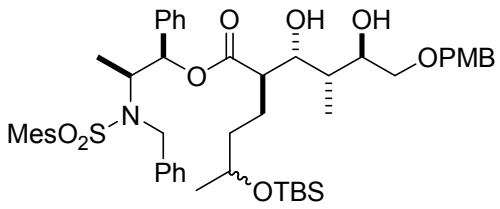


309

(2*R*,3*R*,4*R*,5*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 6-(4-Methoxybenzyloxy)-5-(*tert*-butyldimethylsilyloxy)-2-(3-(*tert*-butyldimethylsilyloxy)butyl)-3-hydroxy-4-methylhexanoate (309)

To a solution of ester **285** (1.06 g, 1.63 mmol) in DCM (8.0 mL) at room temperature was added triethylamine (0.54 mL, 3.90 mmol) and the resulting mixture was cooled to – 78 °C. A solution of dicyclohexylboron triflate (1*M* solution in hexane, 3.58 mL, 3.58 mmol) was added dropwise over 5 min. The resulting cloudy mixture was stirred at – 78 °C for 2 h, at which point a solution of aldehyde **308** (0.57 g, 1.63 mmol) in DCM (4.0 mL) was added dropwise. The reaction mixture was stirred for another 15.5 h at – 78 °C and was allowed to warm to room temperature over 1 h, then quenched by addition of pH 7 buffer solution (8.0 mL). The mixture was diluted with MeOH (40 mL), and 30% hydrogen peroxide (4.0 mL) was added carefully. The reaction mixture was stirred vigorously overnight and concentrated under reduced pressure. The residue was partitioned between water (20 mL) and DCM (40 mL). The aqueous layer was extracted with DCM (3 x 30 mL) and the combined organic extracts were washed with water (3 x 20 mL), dried over anhydrous $NaSO_4$ and filtered. The filtrate was concentrated and the residue was purified by flash

chromatography (5% - 10% EtOAc/hexanes) to provide alcohol **309** (1.14 g, 70%, 88% brsm) as a white foam: IR (neat) 3474 (br),3065, 3033, 2954, 2930, 2857, 1741, 1607, 1587, 1514, 1497, 1471, 1463, 1372, 1325, 1251, 1206, 1155, 1094, 1005, 910, 838, 776, 731, 699, 660, 597, 567 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ (ppm) -0.06 and -0.03 (s, 3H), -0.02 and -0.02 (s, 3H), 0.07 (s, 3H), 0.09 (s, 3H), 0.84 and 0.85 (s, 9H), 0.85 and 0.86 (s, 9H), 0.92 (m, 3H), 0.93-0.98 (m, 2H), 1.08 (m, 3H), 1.09-1.18 (m, 2H), 1.12 (m, 3H), 1.91-1.95 (m, 1H), 2.35 (s, 3H), 2.54 and 2.56 (s, 6H), 2.57-2.65 (m, 1H), 3.45-3.51 (m, 1H), 3.45-3.56, 3.56-3.59 and 3.60-3.62 (m, 2H), 3.81 (s, 3H), 3.88-3.95 (m, 1H), 3.88-4.00 (m, 1H), 4.15-4.20 (m, 1H), 4.44-4.46 (m, 2H), 4.80-4.85 (m, 1H), 5.02-5.08 (m, 1H), 5.61 (m, 1H), 6.66-6.68 (m, 2H), 6.86-6.89 (m, 2H), 6.95-7.00 (m, 2H), 7.01-7.03 (m, 2H), 7.03-7.05 (m, 1H), 7.20-7.27 (m, 5H), 7.48-7.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.8, -4.7, -4.4, -4.3, 9.8, 9.9, 13.4, 13.6, 14.1, 18.0, 20.9, 22.7, 22.9, 23.4, 24.0, 24.5, 25.8, 25.9, 31.6, 34.7, 35.6, 36.4, 37.2, 48.3, 49.6, 50.1, 55.2, 56.8, 67.9, 68.4, 71.7, 72.8, 73.0, 73.2, 74.9, 76.7, 77.1, 77.4, 78.1, 78.4, 126.2, 126.3, 126.7, 127.7, 127.9, 128.0, 128.1, 128.2, 129.4, 129.7, 132.2, 134.0, 134.1, 138.8, 140.0, 140.1, 140.5, 142.4, 159.3, 174.6, 175.1; HRMS (ES) calcd for $C_{56}H_{86}NO_9SSi_2$ $[M+H]^+$ *m/z* 1004.5562, found *m/z* 1004.5648.

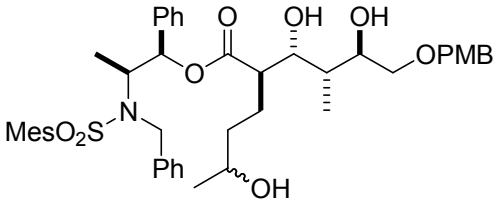


311

(2*R*,3*R*,4*R*,5*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 6-(4-Methoxybenzyloxy)-2-(3-(*tert*-butyldimethylsilyloxy)butyl)-3,5-dihydroxy-4-methylhexanoate (311)

To a stirred mixture of bisTBS ether **309** (100.0 mg, 0.0996 mmol) in DMF (1.24 mL) and water (9.0 μL) at room temperature was added TAS-F (68.6 mg, 0.249 mmol) and the resulting mixture was stirred for 45 min. The reaction mixture was diluted with EtOAc (2.0 mL) and washed with pH 7 buffer (2.0 mL). The aqueous layer was extracted with EtOAc (3 x 2.0 mL) and the combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the residue by flash chromatography (20-40% EtOAc in hexanes) furnished diol **311** (74.6 mg, 84%) as a white solid: IR (neat) 3492 (br), 3063, 3031, 2954, 2929, 2856, 1740, 1611, 1514, 1497, 1456, 1375, 1324, 1250, 1207, 1153, 1099, 1034, 1010, 910, 836, 775, 730, 699, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) -2.03 and -0.02 (s, 3H), -0.01 and 0.00 (s, 3H), 0.85 and 0.86 (s, 9H), 0.89-0.93 (m, 3H), 1.00-1.05 (m, 3H), 1.05-1.75 (m, 5H), 1.19-1.21 (m, 3H), 2.32 (s, 3H), 2.50 and 2.52 (s, 6H), 2.55-2.62 (m, 1H), 2.79-2.81 (m, 1H), 3.04 (s, 1H), 3.50-3.56 (m, 2H), 3.57-3.62 (m, 1H), 3.79-3.85 (m, 1H), 3.82 (s, 3H), 4.02-4.10 (m, 1H), 4.15-4.21 (m,

1H), 4.50 (s, 2H), 4.61-4.71 (m, 1H), 4.80-4.90 (m, 1H), 5.77 (d, J = 4.4 Hz, 1H), 6.75-6.80 (m, 2H), 6.88-6.93 (m, 4H), 7.15-7.28 (m, 8H), 7.37-7.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.8 and -4.7, -4.3, 9.8 and 9.9, 13.7 and 14.0, 18.0, 20.9, 22.9, 23.4, 23.9, 24.7, 25.8, 29.7, 35.8, 36.2, 36.7, 48.2, 49.2 and 49.5, 55.3, 56.7, 68.0 and 68.3, 71.9, 72.1, 72.3, 73.1, 73.9, 78.1 and 78.4, 113.9, 126.5, 127.0, 127.9, 128.0, 128.2, 128.3, 129.3, 129.4, 129.5, 129.9, 132.1, 133.6, 133.7, 138.3, 138.4, 139.1, 139.2, 140.4, 142.4, 159.4, 174.5 and 174.8; HRMS (ES) calcd for $C_{50}H_{72}NO_9SSi$ $[M+H]^+$ m/z 890.4662, found m/z 890.4697.

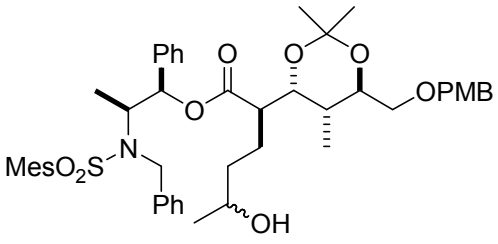


312

(2*R*,3*R*,4*R*,5*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 6-(4-Methoxybenzyloxy)-3,5-dihydroxy-2-(3-hydroxybutyl)-4-methylhexanoate (312)

To a stirred solution of bisTBS ether **309** (126 mg, 0.125 mmol) in THF (2.5 mL) at 0°C was added dropwise HF·py complex (1.40 mL) and the resulting mixture was stirred at 0°C for 30 min, then was allowed to warm to room temperature over 30 min. The reaction mixture was cooled to 0°C and diluted with Et_2O (2.5 mL). The combined organic phases were washed with $NaHCO_3$ (4.0 mL) and the aqueous phase was extracted with Et_2O (4.0 mL). The combined organic layers were washed with

brine (5.0 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (50% EtOAc/hexanes) of the residue provided triol **312** (91 mg, 94%) as a white foam: IR (neat) 3453 (br), 3063, 3025, 2954, 2924, 2854, 1738, 1610, 1514, 1455, 1378, 1318, 1249, 1152, 1034, 1011, 910, 853, 731, 699, 661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.95-0.96 (m, 3H), 1.00-1.02 (m, 3H), 1.21-1.23 (m, 3H), 1.35-1.50 (m, 2H), 1.50-1.63 (m, 2H), 1.72-1.79 (m, 1H), 2.33 (s, 3H), 2.49 (s, 6H), 2.61-2.69 (m, 1H), 3.50-3.56 (m, 3H), 3.79-3.85 (m, 1H), 3.83 (s, 3H), 4.09-4.20 (m, 2H), 4.50 (s, 2H), 4.60-4.69 (m, 1H), 4.80-4.87 (m, 1H), 5.80-5.82 (m, 1H), 6.80-6.83 (m, 2H), 6.89-6.91 (m, 4H), 7.14-7.17 (m, 2H), 7.20-7.29 (m, 6H), 7.36-7.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 9.7, 14.0, 20.9, 22.9, 23.4, 24.9, 25.4, 35.7 and 36.2, 35.8, 48.1, 48.9, 49.4, 55.3, 56.6, 67.3 and 67.6, 71.9 and 72.1, 72.2, 73.1, 73.7, 78.2, 113.9, 126.6, 126.7, 127.1, 128.0, 128.2, 128.3, 129.5, 129.8, 132.1, 133.0, 138.3, 139.0, 140.4, 142.5, 159.4, 174.6 and 174.8; HRMS (ES) calcd for $C_{44}H_{57}NO_9SNa$ $[M+Na]^+$ *m/z* 798.3690, found *m/z* 798.3652.



313

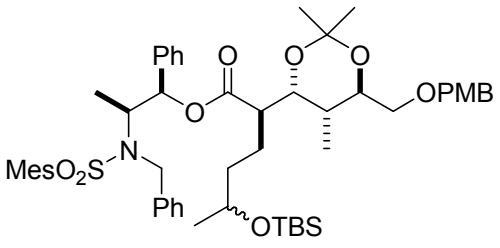
(*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 2-((4*R*,5*R*,6*R*)-6-((4-Methoxybenzyloxy)methyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)-5-hydroxyhexanoate (313)

Method A. To a stirred solution of TBS ether **314** (56.0 mg, 0.0602 mmol) in THF (1.2 mL) at 0 °C was added HF·py (0.25 mL) and the resulting mixture was allowed to warm to room temperature over 2.5 h. The reaction mixture was diluted with Et_2O (2.0 mL), cooled to 0 °C and neutralized with saturated aqueous $NaHCO_3$. The aqueous phase was extracted with Et_2O (3 x 5.0 mL) and the combined organic phases were washed with saturated aqueous NaCl (5.0 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (30-40% EtOAc in hexanes) to give alcohol **313** (47.4 mg, 96%) as a colorless oil.

Method B. To a stirred mixture of triol **312** (407 mg, 0.525 mmol), 2,2-dimethoxypropane (0.10 mL, 0.788 mmol) and 4 Å MS in acetone (10.5 mL) at room temperature was added CSA (24 mg, 0.105 mmol) and the resulting mixture was heated to reflux for 1 h. The solution was cooled to room temperature and filtered. The filtrate was evaporated to give a residue which was diluted with DCM (10 mL), washed with $NaHCO_3$ (5 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (30% EtOAc/hexanes) to deliver cyclic ketal **313** (310 mg, 72%) as a white foam.

Method C. To a stirred mixture of triol **312** (218 mg, 0.281 mmol) and 2,2-dimethoxypropane (0.10 mL, 0.844 mmol) in DCM (7.0 mL) at room temperature was added PPTS (9.9 mg, 0.0394 mmol), and the resulting mixture was heated at reflux for 3 h. The solution was cooled and the reaction mixture was quenched with saturated

aqueous $NaHCO_3$ (7.0 mL). The aqueous phase was extracted with DCM (2 x 10.0 mL) and the organic phase was dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash chromatography (30% EtOAc/hexanes) to deliver cyclic ketal **313** (245 mg, quant.) as a white foam: IR (neat) 3470 (br), 3063, 3031, 2965, 2924, 2853, 1741, 1610, 1513, 1458, 1379, 1320, 1247, 1224, 1153, 1034, 1011, 930, 910, 854, 821, 732, 699, 660, 598, 567 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.94-0.97 (m, 6H), 1.10-1.13 (m, 3H), 1.28-1.32 (m, 6H), 1.30-1.52 (m, 4H), 1.60-1.70 (br s, 1H) 1.75-1.85 (m, 1H), 2.36 (s, 3H), 2.49 and 2.50 (s, 6H), 2.57-2.70 (m, 1H), 3.40-3.52 (m, 4H), 3.82 (s, 3H), 3.90-4.02 (m, 2H), 4.01-4.55 (m, 2H), 4.56-4.61 and 4.91-4.97 (m, 2H), 5.74-5.75 (m, 1H), 6.67-6.71 (m, 2H), 6.89-6.91 (m, 2H), 6.95-6.96 (m, 2H), 7.09-7.12 (m, 2H), 7.18-7.19 (m, 1H), 7.26-7.32 (m, 5H), 7.46-7.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 11.9 and 12.0, 14.1 and 14.2, 21.0, 22.9, 23.5 and 23.6, 23.7, 24.3 and 25.1, 24.7, 34.1, 36.1 and 36.7, 46.3 and 46.9, 48.1, 55.3, 46.5, 66.8 and 67.5, 70.7 and 70.8, 71.4, 73.1, 74.5, 78.1 and 78.2, 101.3, 113.8, 126.6 and 126.7, 127.3, 128.0, 128.1, 128.3, 128.4, 129.3, 130.3, 132.2, 133.4, 138.4, 139.2 and 139.3, 140.4, 142.5, 159.2, 173.9 and 174.2; HRMS (ES) calcd for $C_{47}H_{62}NO_9S$ $[M+H]^+$ *m/z* 816.4145, found *m/z* 816.4174.

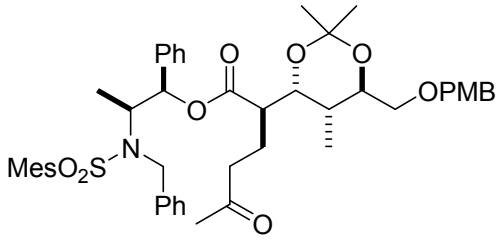


314

(*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 2-((4*R*,5*R*,6*R*)-6-((4-Methoxybenzyloxy)methyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)-5-(*tert*-butyldimethylsilyloxy)hexanoate (314)

To a stirred solution of diol **311** (13.0 mg, 0.0146 mmol), 2,2-dimethoxypropane (2.7 μL, 0.0219 mmol) and 4 Å MS in acetone (0.30 mL) at room temperature was added CSA (0.5 mg, 0.00146 mmol) and the resulting mixture was stirred for 3.0 h. The reaction mixture was filtered and the filtrate was evaporated to give a residue which was diluted with DCM (2.0 mL), washed with $NaHCO_3$ (2.0 mL), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash chromatography (20% EtOAc/hexanes) to deliver cyclic ketal **314** (11.2 mg, 82%) as a colorless oil: IR (neat) 3063, 3025, 2954, 2929, 2856, 1743, 1607, 1514, 1456, 1380, 1326, 1248, 1224, 1153, 1036, 1011, 909, 836, 775, 730, 699, 672, 660 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ (ppm) -0.04 and -0.03 (s, 6H), 0.84 and 0.86 (s, 9H), 0.92-0.94 (m, 3H), 0.96-0.98 (m, 3H), 1.06-1.10 (m, 3H), 1.20-1.39 (m, 4H), 1.29-1.35 (m, 6H), 1.82-1.84 (m, 1H), 2.36 (s, 3H), 2.51 and 2.54 (s, 6H), 2.59-2.63 (m, 1H), 3.48-3.51 (m, 1H), 3.49-3.51 and 3.61-3.65 (m, 1H), 3.56-3.57 (m, 2H), 3.83 (s, 3H), 3.88-3.92 (m, 1H), 4.04 (dd, *J* = 11.2, 4.8 Hz, 1H), 4.51-4.56 (m, 2H), 4.57-4.62 and 4.99-5.03 (m, 2H), 5.70-5.72 (m, 1H), 6.65-6.68 (m, 2H), 6.89-6.91 (m, 2H), 6.97-6.99 (m, 2H), 7.09-7.13 (m, 2H), 7.16-7.20 (m, 1H), 7.24-7.31 (m, 5H), 7.49-7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -4.8 and -4.7, -4.4 and -4.3, 11.9 and 12.0, 13.8 and 14.1, 17.9 and 18.0, 20.9, 22.9, 23.2, 23.8, 23.9, 24.7, 25.3, 25.8, 29.7, 34.1 and 34.2, 36.6 and 37.4, 46.9 and 47.2, 48.1 and 48.2, 55.3,

56.7, 67.8 and 68.2, 70.6 and 70.9, 71.5, 73.0, 74.5 and 74.6, 78.1 and 78.4, 101.3, 113.8, 126.4 and 126.5, 127.1 and 127.2, 127.8, 128.0, 128.1, 128.3, 128.4, 129.2, 130.4, 132.2, 133.6 and 133.7, 138.4 and 138.5, 139.4 and 139.5, 140.4, 142.4, 159.2, 173.8 and 174.1; HRMS (ES) calcd for $C_{53}H_{75}NO_9SSiNa$ $[M+Na]^+$ *m/z* 952.4988, found *m/z* 952.4830.

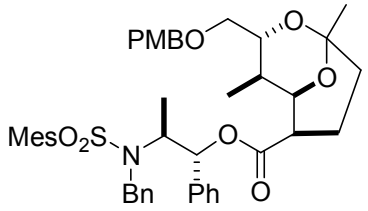


315

(*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 2-((4*R*,5*R*,6*R*)-6-((4-Methoxybenzyloxy)methyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)-5-oxohexanoate (315)

To a stirred mixture of alcohol **313** (300 mg, 0.368 mmol) and $NaHCO_3$ (93 mg, 1.103 mmol) in DCM (18 mL) at room temperature was added DMP (234 mg, 0.551 mmol) and the resulting mixture was stirred for 30 min. The reaction mixture was quenched with H_2O (18 mL) and the aqueous phase was extracted with DCM (2 x 25 mL). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (30% EtOAc/hexanes) of the crude product provided ketone **315** (302 mg, quant.) as a white solid: mp. 153-155 °C; $[\alpha]_D^{20}$ +35.2 (*c* 1.00, $CHCl_3$); IR (neat) 3058, 3025, 2924, 2854, 1740, 1718, 1610, 1513, 1456, 1380, 1322, 1247, 1153, 1035, 1011, 909, 854, 731, 699, 660 cm^{-1}; ^1H

NMR (400 MHz, $CDCl_3$) δ (ppm) 0.99 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.29 (s, 3H), 1.31 (s, 3H), 1.40-1.51 (m, 1H), 1.67-1.76 (m, 1H), 1.81-1.83 (m, 1H), 1.82 (s, 3H), 2.03 (t, *J* = 7.6 Hz, 2H), 2.36 (s, 3H), 2.47 (s, 6H), 2.65 (dt, *J* = 3.6, 11.2 Hz, 1H), 3.46-3.55 (m, 3H), 3.83 (s, 3H), 3.97-4.01 (m, 2H), 4.51-4.56 (m, 2H), 4.58 and 4.90 (AB quartet, 2H), 5.78 (d, *J* = 5.6 Hz, 1H), 6.73 (d, *J* = 7.2 Hz, 2H), 6.89 (d, *J* = 7.2 Hz, 2H), 6.94 (s, 2H), 7.12-7.16 (m, 2H), 7.23-7.31 (m, 6H), 7.41-7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 11.8, 14.4, 20.9, 22.1, 22.9, 23.7, 24.7, 29.6, 34.1, 40.0, 45.8, 48.0, 55.3, 56.3, 70.7, 71.5, 73.0, 74.6, 77.8, 101.3, 113.8, 126.9, 127.3, 128.1, 128.2, 128.3, 128.6, 129.3, 130.4, 132.2, 133.3, 138.4, 138.9, 140.5, 142.6, 159.2, 173.7, 206.9; HRMS (ES) calcd for $C_{47}H_{59}NO_9SNa$ $[M+Na]^+$ *m/z* 836.3808, found *m/z* 836.3759.

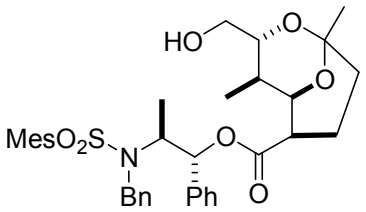


316

(4*R*,5*R*,6*R*,7*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 7-((4-Methoxybenzyloxy)methyl)-1,6-dimethyl-8,9-dioxa-bicyclo[3.3.1]nonane-4-carboxylate (316)

To a stirred solution of ketone **315** (280 mg, 0.344 mmol) in benzene (17 mL) was added *p*-TsOH·H_2O (7 mg, 0.034 mmol) and the resulting mixture was stirred for 8 h at room temperature. The reaction mixture was quenched with saturated aqueous

$NaHCO_3$ (10 mL) and the aqueous phase was extracted with DCM (20 mL). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. Flash chromatography (10-20% EtOAc/hexanes) of the crude product provided cyclic ketal **316** (234 mg, 90%) as a white foam. $[\alpha]_D^{20}$ +8.2° (*c* 1.00, $CHCl_3$); IR (neat) 3058, 3031, 2982, 2938, 2851, 1737, 1610, 1513, 1496, 1455, 1381, 1324, 1248, 1152, 1101, 1055, 1032, 931, 912, 859, 818, 763, 731, 699, 672, 658 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.40 (d, *J* = 7.2 Hz, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.35 (s, 3H), 1.71-1.80 (m, 1H), 1.83-1.95 (m, 1H), 2.05-2.25 (m, 3H), 2.30 (s, 3H), 2.42 (s, 6H), 2.79-2.83 (m, 1H), 3.29-3.32 (m, 1H), 3.49-3.43 (m, 1H), 3.82 (s, 3H), 4.10-4.15 (m, 1H), 4.15-4.19 (m, 1H), 4.35-4.39 (m, 1H), 4.46 and 4.68 (AB quartet, *J* = 16.4 Hz, 2H), 4.51 (s, 2H), 5.78 (d, *J* = 6.4 Hz, 1H), 6.85-6.91 (m, 6H), 7.10-7.15 (m, 2H), 7.19-7.29 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.5, 14.8, 20.9, 22.2, 22.9, 29.4, 33.3, 34.0, 44.1, 48.1, 55.3, 56.5, 72.0, 72.5, 73.1, 76.4, 78.2, 95.1, 113.8, 127.0, 127.5, 127.9, 128.1, 128.2, 128.4, 129.3, 130.4, 132.1, 133.0, 137.5, 138.1, 140.4, 142.5, 159.2, 170.7; HRMS (ES) calcd for $C_{44}H_{53}NO_8SNa$ $[M+Na]^+$ *m/z* 778.3390, found *m/z* 778.3414.

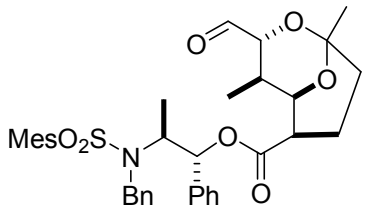


317

(4*R*,5*R*,6*R*,7*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 7-(Hydroxymethyl)-1,6-dimethyl-8,9-dioxa-bicyclo[3.3.1]nonane-4-carboxylate (317)

To a stirred solution of PMB ether **316** (14.5 mg, 19.2 μmol) and DDQ (6.6 mg, 28.8 μmol) in DCM (0.95 mL) at room temperature was added H_2O (0.05 mL) and the resulting brown-green solution was stirred for 1.5 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (3.0 mL) and the aqueous layer was extracted with DCM (3 x 3.0 mL). The organic layer was washed with water (6.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (30% EtOAc/hexanes) to afford alcohol **317** (12 mg, 98%) as a colorless oil: $[\alpha]_D^{26}$ +16.2 (*c* 1.00, $CHCl_3$); IR (neat) 3492 (br), 3063, 3025, 2939, 1737, 1604, 1496, 1454, 1382, 1324, 1207, 1152, 1125, 992, 930, 860, 758, 699, 658 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.40 (d, *J* = 7.0 Hz, 3H), 1.27 (d, *J* = 4.2 Hz, 3H), 1.33 (s, 3H), 1.77-1.82 (m, 1H), 1.91-1.95 (m, 1H), 2.01-2.10 (m, 1H), 2.15-2.27 (m, 2H), 2.30 (s, 3H), 2.42 (s, 6H), 2.80-2.85 (m, 1H), 3.30-3.36 (m, 1H), 3.59-3.62 (m, 1H), 4.04-4.08 (m, 1H), 4.19-4.22 (m, 1H), 4.38-4.41 (m, 1H), 4.45 (A of AB quartet, *J* = 16.4 Hz, 1H), 4.67 (B of AB quartet, *J* = 16.4 Hz, 1H), 5.80 (d, *J* = 6.0 Hz, 1H), 6.85 (s, 2H), 6.91 (d, *J* = 7.2 Hz, 2H), 7.14-7.16 (m, 2H), 7.25-7.29 (m, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) 12.3, 14.8, 20.9, 22.0, 22.9, 29.2, 29.7, 32.0, 34.0, 43.8, 48.1, 56.4, 64.3, 71.8, 76.7, 78.2, 95.2, 127.0, 127.5, 127.9, 128.2, 128.3, 128.5, 132.2, 132.9, 137.4, 138.1, 140.4, 142.6,

170.5; HRMS (ES) calcd for $C_{36}H_{45}NO_7SNa$ $[M+Na]^+$ *m/z* 658.2814, found *m/z* 658.2801.



318

(4*R*,5*R*,6*R*,7*R*)-((1*R*,2*S*)-2-(*N*-Benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl) 7-Formyl-1,6-dimethyl-8,9-dioxa-bicyclo[3.3.1]nonane-4-carboxylate (318)

Method A. To a stirred mixture of alcohol **317** (300 mg, 0.368 mmol) and $NaHCO_3$ (93 mg, 1.103 mmol) in DCM (18 mL) at room temperature was added DMP (234 mg, 0.551 mmol) and the resulting cloudy mixture was stirred for 30 min, then quenched with H_2O (18 mL). The aqueous phase was extracted with DCM (2 x 25 mL) and the organic phase was washed with brine (30 mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to leave a crude product which was purified by flash chromatography (30% EtOAc/hexanes) to give aldehyde **318** (302 mg, quant.) as a white foam.

Method B. To a stirred solution of oxalyl chloride (27 μL, 0.301 mmol) in DCM (3.0 mL) at -78 °C was added dropwise a solution of DMSO (43 μL, 0.602 mmol) in DCM (1.2 mL) and the resulting mixture was stirred for 10 min, at which

point a solution of alcohol **317** (160 mg, 0.252 mmol) in DCM (2.5 mL) was added slowly. The solution was stirred at -78 °C for 20 min and Et_3N (0.19 mL) was added dropwise. The mixture was stirred for 10 min then was slowly allowed to warm to room temperature. The reaction mixture was quenched with water (6.0 mL) and the aqueous layer was extracted with DCM (6.0 mL). The organic layer was washed with brine (6.0 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography (25% EtOAc/Hexanes) to provide aldehyde **318** (156 mg, 93%) as a colorless viscous oil: $[\alpha]_D^{26}$ +29.8 (*c* 1.00, $CHCl_3$); IR (neat) 3069, 3031, 2940, 2851, 2813, 1738, 1604, 1496, 1454, 1382, 1324, 1206, 1153, 1124, 1012, 930, 910, 860, 763, 731, 699, 658 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.44 (d, *J* = 7.7 Hz, 3H), 1.27 (d, *J* = 4.2 Hz, 3H), 1.39 (s, 3H), 1.76-1.82 (m, 1H), 1.95-2.01 (m, 1H), 2.06-2.12 (m, 2H), 2.22-2.27 (m, 1H), 2.30 (s, 3H), 2.45 (s, 6H), 2.75-2.78 (m, 1H), 4.18-4.22 (m, 2H), 4.44-4.45 (m, 1H), 4.47 (A of AB quartet, *J* = 16.1 Hz, 1H), 4.65 (B of AB quartet, *J* = 16.1, 1H), 5.82 (d, *J* = 5.6 Hz, 1H), 6.85 (s, 2H), 6.94 (d, *J* = 7.7 Hz, 2H), 7.17 (t, *J* = 7.7 Hz, 2H), 7.23-7.29 (m, 6H), 9.33 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) 11.6, 14.7, 20.9, 21.6, 22.9, 28.9, 30.4, 34.0, 43.6, 48.1, 56.3, 71.2, 78.3, 80.6, 95.1, 127.0, 127.5, 127.8, 128.3, 128.5, 132.2, 132.9, 137.2, 138.1, 140.3, 142.6, 170.1, 200.0; HRMS (ES) calcd for $C_{36}H_{43}NO_7SNa$ $[M+Na]^+$ *m/z* 656.2658, found *m/z* 656.2634.

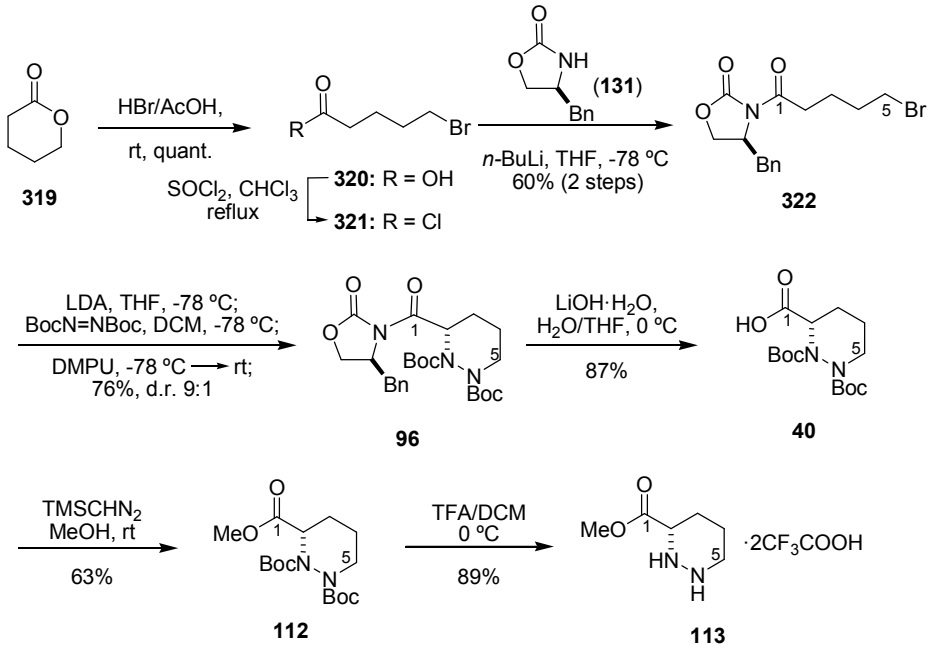
CHAPTER 4: SYNTHESIS OF THE C1-N12 TRIPEPTIDE OF SANGLIFEHRIN A

Our route to the C1-N12 tripeptide **241** of SFA first required preparation of piperazic acid derivative **113** and *(S)*-*m*-hydroxyphenylalanine derivative **244**. The latter would be linked with L-valine via racemization-free peptide synthesis to form tripeptide **241** which would be used for fabrication of a C1-C19 substructure by coupling with carboxylic acid **242**. Synthesis of the components of **241** and their assembly into the complete tripeptide are described in the sections that follow.

4.1 Synthesis of Piperazic Acid Methyl Ester 113

Following Hale's protocol,[1] the synthesis of piperazic acid methyl ester **113** commenced with treatment of δ-valerolactone (**319**) with hydrobromic acid in acetic acid to give 5-bromopentanoic acid **320** (Scheme 4.1). The carboxyl group of **320** was activated with thionyl chloride in refluxing chloroform and the resultant acyl chloride **321** was condensed with *(S)*-oxazolidinone **131** to afford *N*-acylated oxazolidinone **322**. Enolization of **322** was accomplished using Evans' procedure,[2] wherein a precooled solution of the oxzolidinone in tetrahydrofuran was added to lithium diisopropylamide in tetrahydrofuran at −78 °C. The resulting mixture was treated with di-*tert*-butyl azodicarboxylate in dichloromethane at −78 °C, then with 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone, and the frozen reactants were allowed to

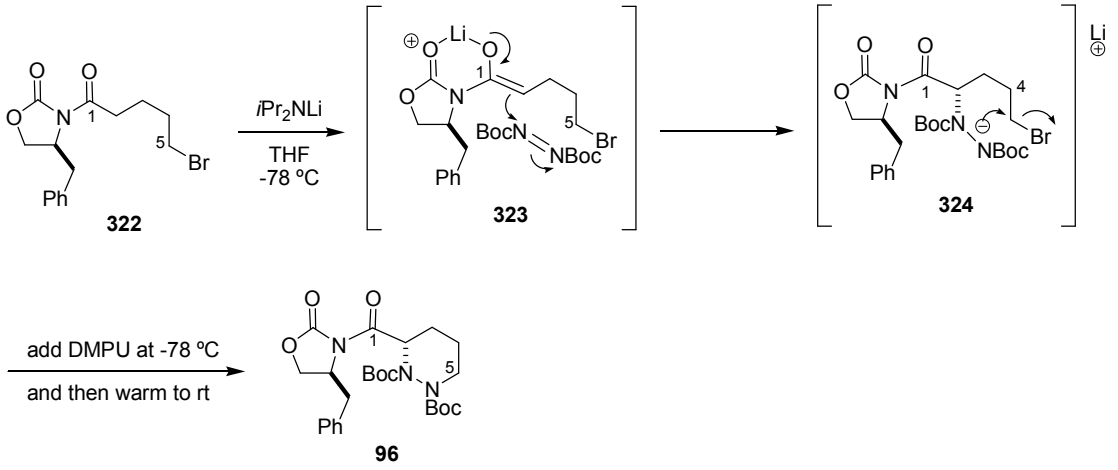
warm to room temperature. This one-pot procedure provided **96** in 76% yield and 90% diastereomeric ratio.



Scheme 4.1 Synthesis of piperazic acid methyl ester **113** (22% yield, *7 steps*)

The mechanism for the transformation of bromide **322** into **96** is illustrated in Scheme 4.2 and rationalizes how the *(S)*-oxazolidinone in enolate **323** directs attack by di-*tert*-butyl azodicarboxylate to the re face of the enolate and leads to intermediate **324**. Intramolecular displacement of bromide from **324** occurs after addition of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone at -78 ºC to produce **96**. The oxazolidinone auxiliary was removed from **96** by treatment with lithium hydroxide in wet tetrahydrofuran and the resultant carboxylic acid **40** was esterified with trimethylsilyldiazomethane to deliver methyl ester **112** (Scheme 4.1). The pair of *tert*-

butoxycarbonyl protecting groups was removed from **112** by treatment with trifluoroacetic acid to yield piperazic acid methyl ester **113** as its bis-trifluoroacetate.

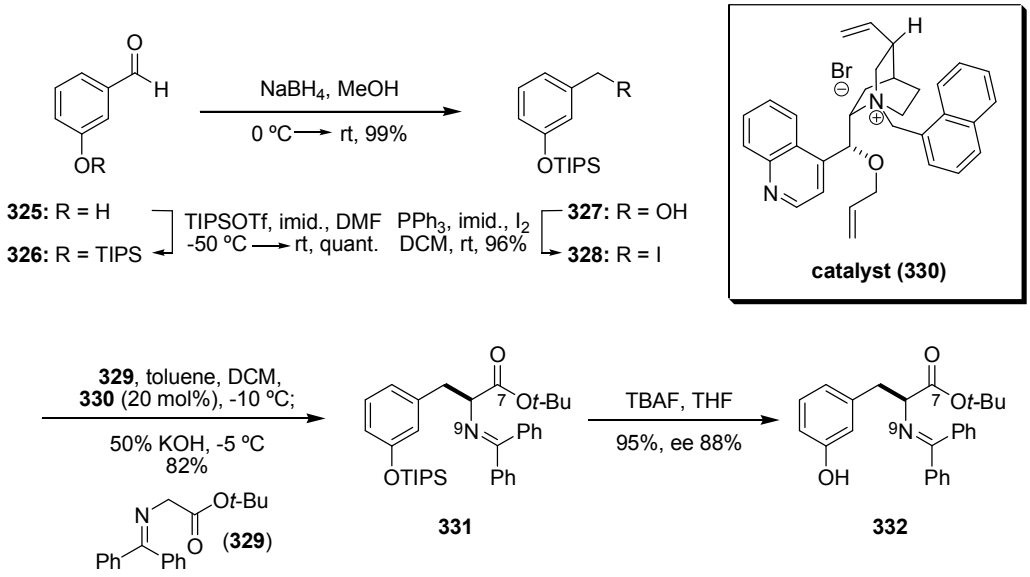


Scheme 4.2 Mechanism for enantioselective formation of **96**

4.2 Synthesis of *(S)-m*-Hydroxyphenylalanine Derivative 244

While synthesis of piperazic acid methyl ester **113** was in progress, the synthesis of *(S)-m*-hydroxyphenylalanine derivative **244** was explored using an asymmetric catalytic phase-transfer method for introducing the α-amino function[3] (Scheme 4.3). First, the phenolic hydroxyl group of 3-hydroxybenzaldehyde (**325**) was masked with triisopropylsilyl trifluoromethanesulfonate to give silyl ether **326**[4] which was reduced with sodium borohydride in methanol to primary alcohol **327**.[5] Treatment of **327** with a mixture of iodine and triphenylphosphine in the presence of imidazole gave iodide **328**,[6] and this was reacted with imino ester **329** in the presence of phase-transfer catalyst **330** in a mixture of dichloromethane and toluene at −10 °C and then

with 50% aqueous potassium hydroxide. This afforded *tert*-butyl ester **331** in good yield. The enantioselectivity of this reaction results from the transition state shown in Figure 4.1 where an ion pair is formed between the enolate of imino ester **329** and catalyst **330**. This configuration is the lowest energy transition state due to direction-specific ion pairing which brings the enolate oxygen into proximity with the less sterically hindered face of the bridgehead quaternary nitrogen atom. A π-stacking interaction between the isoquinoline moiety and the enolate double bond helps stabilize this orientation. The alkyl halide **328** approaches the enolate in this complex from the more accessible *si* face leading to the *(S)*-product **331**.[3] The enantiomeric excess of **331** could not be determined by chiral high-performance liquid chromatography and therefore **331** was converted to **332** in which the enantiomeric excess was determined to be 88% by chiral high-performance liquid chromatography. Attempts to conduct the phase-transfer reaction of **329** with the bromide and chloride analogs of iodide **328** in the presence of **330** were unsuccessful.



Scheme 4.3 Synthesis of imine **331** using asymmetric phase-transfer catalysis (78% yield, *4 steps*)

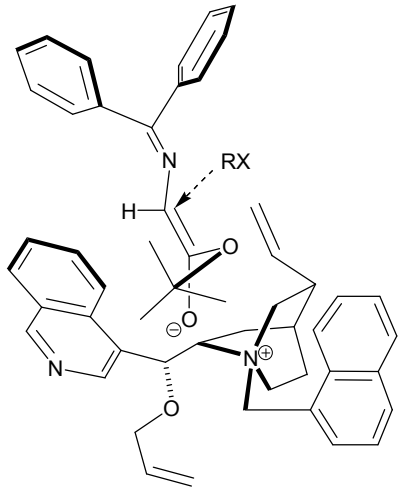
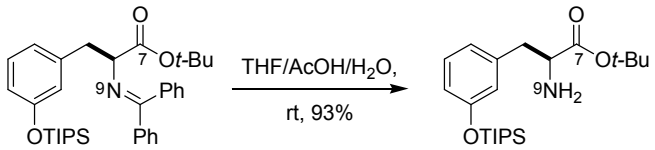


Figure 4.1 Stereoview of the ion pair formed between the enolate of imino ester **329** and catalyst **330**

With **331** in hand, hydrolysis of the imine was attempted with 12*M* hydrochloric acid in warm acetonitile (40 °C) but these conditions led only to decomposition of **331**. Treatment of **331** with dilute hydrochloric acid (1*M*) resulted in a low yield (12%) of amino ester **244** but when **331** was exposed to a mixture of 1:1:1 acetic acid-tetrahydrofuran-water amino ester **244** was produced in excellent yield (Scheme 4.4).



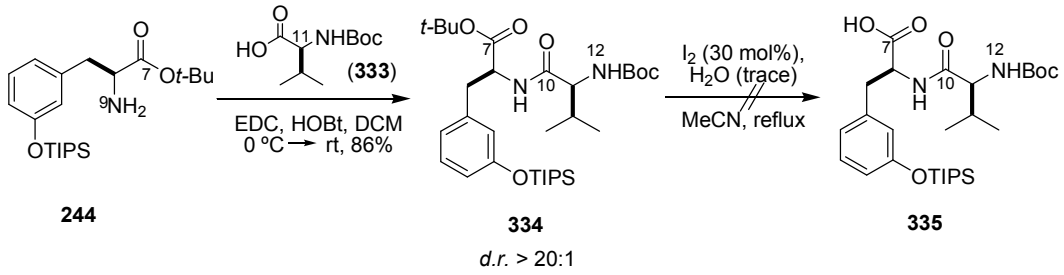
331 **244**

Scheme 4.4 Hydrolysis of imine **331** to *(S)-m*-hydroxyphenylalanine derivative **244**

4.3 Synthesis of the C7-C19 Segment of SFA

In our initial approach to the C1-N12 tripeptide **241**, we planned to link piperazic acid methyl ester **113** with carboxylic acid **335**, and to this end coupling of *(S)-m*-hydroxyphenylalanine derivative **244** with commercially available *tert*-butoxycarbonyl-L-valine (**333**) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and 1-hydroxybenzotriazole gave dipeptide **334** in good yield and high diastereomeric ratio (Scheme 4.5). Unfortunately, attempts to effect selective hydrolysis of the *tert*-butyl ester from dipeptide **334** under conditions published by Yadav[7] resulted in recovered starting material with no evidence for formation of **335** (Scheme 4.5). This failure led to a new pathway which avoided the

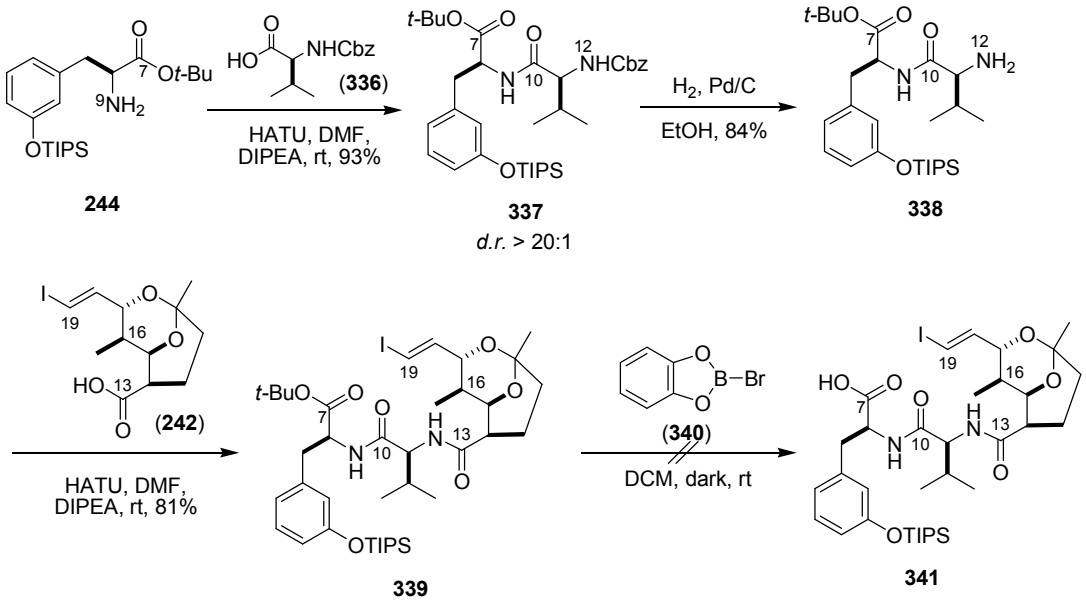
need for selective cleavage of a *tert*-butyl ester in the presence of a *tert*-butoxycarbonyl group by replacing **333** with *N*-carbobenzyloxzy-L-valine (**336**).



Scheme 4.5 Synthesis of dipeptide **334**

In this modified route, **336** was merged with **244** in the presence of *N,N,N′,N′*-tetramethyl-*O*-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate to afford dipeptide **337** in excellent yield and good diastereomeric ratio (Scheme 4.6). Subjection of **337** to palladium-catalyzed hydrogenolysis under atmospheric pressure gave amine **338** and subsequent coupling of **338** with carboxylic acid **242** in the presence of *N,N,N′,N′*-tetramethyl-*O*-(7-azabenzotriazol-1-yl)uronium hexafluoro-phosphate at ambient temperature provided *tert*-butyl ester **339**. At this point, cleavage of the *tert*-butyl ester of **339** was required for linkage of the C7-C19 carboxylic acid **341** with piperazic acid methyl ester **113**. It was obvious that acidic hydrolysis of the *tert*-butyl ester of **339** in the presence of an acid labile cyclic ketal moiety was impractical and an alternative method for this transformation was therefore sought. Bromocatecholborane (**340**)[8] has been used to cleave protecting groups such as methoxyethoxymethyl ethers, *N*-carbobenzyloxy groups and *tert*-butyl esters in peptide synthesis,[9] and this reagent was tested with **339**. However, after several

experiments, we could find no evidence for the formation of **341**; decomposition of the starting material was the sole outcome from this reaction, probably a consequence of the sensitivity of the cyclic ketal towards **340**.



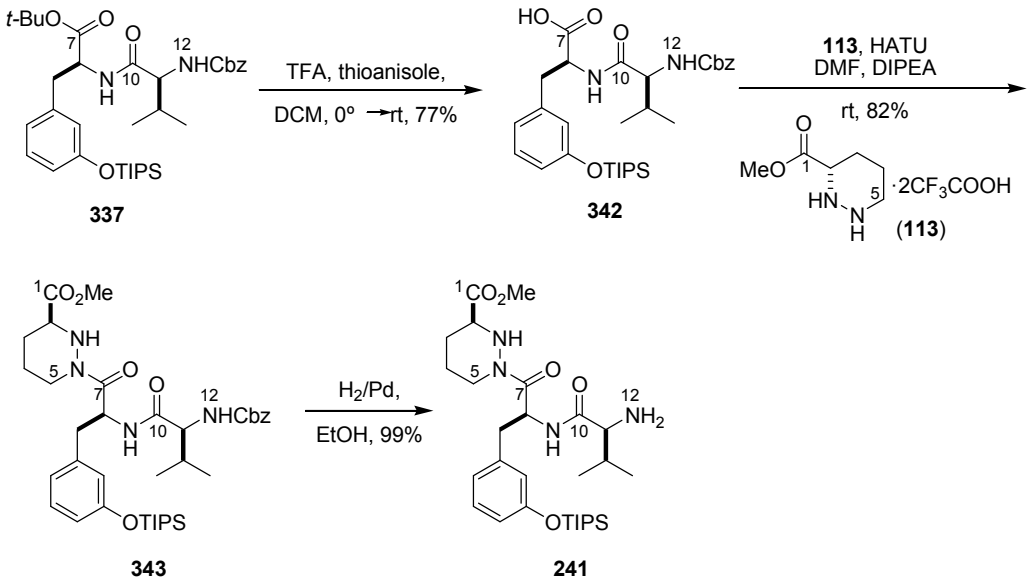
Scheme 4.6 Synthesis of the C7-C19 subunit **339** (63% yield, *3 steps*)

Our failure to cleave the *tert*-butyl ester in **334** and **339** caused us to terminate this route to the C7-C19 subunit of SFA in favor of one that avoided complications associated with the internal ketal moiety. To that end, a new goal was set that accomplished ester hydrolysis at dipeptide **337**.

4.4 Synthesis of the C1-N12 Tripeptide of SFA

Our new route focused on the C1-N12 tripeptide **241** and began with cleavage of *tert*-butyl ester **337** using trifluoroacetic acid and thioanisole to give carboxylic acid

342[10] (Scheme 4.7). The presence of excess thioanisole, a carbocation scavenger, is important for this reaction since acid-catalyzed cleavage of *tert*-butyl esters of amino acids containing an electron-rich aromatic moiety can lead to products with a *tert*-butyl group substituted on the aromatic ring in the absence of a carbocation trap. Carboxylic acid **342** was reacted with piperazic acid methyl ester **113** in the presence of *N,N,N′,N′*-tetramethyl-*O*-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate at ambient temperature to provide tripeptide **343**; subsequent palladium-catalyzed hydrogenolysis of **343** in ethanol under atmospheric pressure funished **241**. This sequence completed the synthesis of tripeptide **241** in 18% overall yield from **319** with a longest linear sequence of nine steps. Importantly, it left a free amino group at the terminus of **241** for linkage with carboxylic acid **242**.



Scheme 4.7 Synthesis of tripeptide **241** from dipeptide **337** (63% yield, *3 steps*)

Synthesis of the C1-N12 tripeptide subunit of sanglifehrin A in this chapter was optimized in terms of peptide coupling efficiency and deprotection methodology. The synthesis of imino ester **331** employed a phase-transfer reaction in the presence of cinchodinium bromide catalyst **330** that afforded useful for the introduction of the amino function and a good yield of the product in high enantiomeric excess. The method offers a valuable and potentially general method for the synthesis of α-amino acids from alkyl halides.

4.5 References

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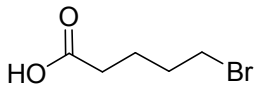
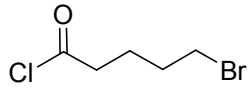
4.6 Experimental Section



320

5-Bromopentanoic Acid (320)

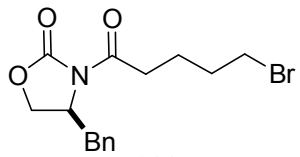
To a solution of 33% HBr in AcOH (0.50 mL) at room temperature was added δ-valerolactone **319** (100 mg, 0.999 mmol) and the resulting mixture was stirred for 26.5 h. The yellow solution was quenched with water (1 mL), extracted with EtOAc (2 x 2 mL), washed with water (2 mL) and brine (2 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide crude carboxylic acid **320** (196 mg, quant.) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.79-1.97 (m, 4H), 2.42 (t, *J* = 9.6, 2H), 3.44 (d, *J* = 8.8 Hz, 2H), 10.82-11.48 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 23.2, 31.8, 32.9, 33.0, 179.3. The carboxylic acid was used in the next step without purification.



321

5-Bromopentanoyl Chloride (321)

To a stirred solution of 5-bromopentanoic acid (**320**, 3.073 g, 16.98 mmol) in $CHCl_3$ (100 mL) at room temperature was slowly added $SOCl_2$ (2.8 mL, 33.96 mmol) over a period of 10 min. The resulting mixture was heated at reflux for 15 h to give the crude acyl chloride **321** (3.172 g, ca. 94%) as a dark yellow oil: IR (neat) 2960, 2871, 1817, 1746, 1452, 1411, 1359, 1255, 1045, 742, 681 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.85-1.93 (m, 4H), 2.97 (t, *J* = 6.9 Hz, 2H), 3.433 (t, *J* = 6.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 23.6, 31.1, 32.4, 46.1, 173.4. The acyl chloride was used in the next step without purification.

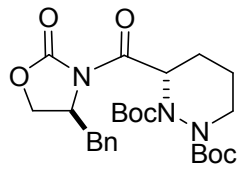


322

(*S*)-4-Benzyl-3-(5-bromopentanoyl)oxazolidin-2-one (322)

To a stirred solution of oxazolidinone **131** (2.56 g, 14.46 mmol) in THF (54 mL) at – 78 °C was added *n*-BuLi (2.6*M* solution in hexane, 5.84 mL, 15.18 mmol) and the resulting mixture was stirred at – 78 °C for 20 min, at which point acyl choride **321** (3.17 g, 15.90 mmol) was added dropwise. After stirring for 2.5 h, the reaction mixture was allowed to warm to room temperature and quenched with saturated aqueous NH_4Cl (15 mL). DCM (60 mL) was added followed by 10% NaOH (30 mL) and the aqueous layer was extracted with DCM (3 x 30 mL). The combined organic extracts were washed with brine (40 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash

chromatography (1:6 EtOAc/hexanes) to provide bromide **322** (3.14 g, 64%) as a white solid: mp. 56-58 °C; $[\alpha]_D^{26}$ +43.6 (*c* 1.00, $CHCl_3$), $[\alpha]_D^{25}$ +78.5 (*c* 1.00, MeOH); IR (neat) 3062, 3028, 2923, 2869, 1780, 1699, 1604, 1497, 1480, 1454, 1389, 1352, 1290, 1213, 1105, 1076, 1051, 1013, 762, 747, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.85-2.07 (m, 4H), 2.80 (dd, *J* = 9.6, 13.6 Hz, 1H), 2.92-3.08 (m, 2H), 3.32 (dd, *J* = 3.2, 13.6 Hz, 1H), 3.48 (t, *J* = 6.4 Hz, 2H), 4.19-4.26 (m, 2H), 4.67-4.73 (m, 1H), 7.22-7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 22.8, 32.0, 33.2, 34.6, 38.0, 55.2, 66.3, 127.4, 129.0, 129.4, 135.2, 153.2, 153.5, 172.6; HRMS (EI) calcd for $C_{15}H_{18}NBrO_3$ $[M]^+$ *m/z* 339.0470, found *m/z* 339.0468.

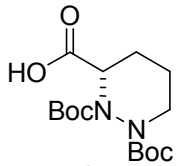


96

(*S*)-di-*tert*-Butyl 3-((*S*)-4-Benzyl-2-oxooxazolidine-3-carbonyl)piperazine-1,2-dicarboxylate (96)

To a stirred solution of bromide **322** (2.57 g, 7.56 mmol) in THF (9.3 mL) at – 78 °C was added dropwise a freshly prepared LDA solution (1*M* solution in THF, 8.32 mL, 8.32 mmol) and the resulting mixture was stirred at – 78 °C for 55 min, at which point a precooled (– 78 °C) solution of DBAD (2.09 g, 9.07 mmol) in DCM (13.6 mL) was added in one portion *via* cannula. After stirring the solution at – 78 °C for 1 h, DMPU (23.7 mL, 197 mmol) was added dropwise over 1 h. By the end of the

addition, the reaction mixture had frozen. The reaction mixture was slowly warmed to room temperature and was stirred for 6 h, then added to Et_2O (190 mL) layered on top of saturated aqueous KH_2PO_4 (70 mL). The two layers were briefly but vigorously shaken and the aqueous phase was extracted with Et_2O (3 x 70 mL). The combined ether layers were washed with saturated aqueous $NaHCO_3$ (70 mL) amd H_2O (120 mL), then dried over anhydrous $MgSO_4$ and filtered. The solvent was removed *in vacuo* to afford a yellow oily residue which was purified by flash chromatography (1:1 Et_2O/hexanes) to provide **96** (2.80 g, 76%) as a white foam: $[\alpha]_D^{30}$ +29.0 (*c* 1.00, MeOH); IR (neat) 3055, 3022, 2978, 2932, 2853, 1783, 1698, 1478, 1455, 1393, 1367, 1296, 1253, 1220, 1166, 1111, 1071, 1049, 1031, 988, 911, 881, 854, 823, 753, 737, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.50 (m), 1.70-2.20 (m), 2.60-2.71 (m), 2.90 (br s), 3.95 (br s), 4.10-4.25 (m), 4.70 (br s), 5.80 (br s), 6.05 (br s), 7.20-7.49 (m); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 28.1, 28.2, 37.6, 55.6, 66.5, 80.3, 81.3, 127.4, 129.0, 129.4, 135.2, 152.6, 170.4; HRMS (CI) calcd for $C_{25}H_{35}N_3O_7$ $[M]^+$ *m/z* 489.2475, found *m/z* 489.2481.

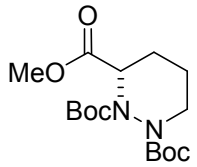


40

(*S*)-1,2-Bis(*tert*-butoxycarbonyl)piperazine-3-carboxylic Acid (40)

To a stirred solution of **96** (2.22 g, 4.53 mmol) in THF (17.8 mL) at – 5 °C was added a solution of lithium hydroxide monohydrate (438 mg, 10.43 mmol) in H_2O (8.9

mL) and the resulting mixture was stirred vigorously for 2 h at 0 °C. The reaction mixture was diluted with water (22 mL) and the aqueous layer was extracted with Et_2O (3 x 55 mL). The organic extracts were washed with saturated aqueous $NaHCO_3$ (55 mL) and the aqueous layers were combined, acidified to pH 2 with solid $NaHSO_4$, and extracted with EtOAc (3 x 110 mL). The organic extract was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford carboxylic acid **40** (1.31 g, 87%) as white prisms: mp. 103-106 °C; $[\alpha]_D^{26}$ -18.2 (*c* 1.00, MeOH); IR (neat) 3200-2500 (br), 2979, 2934, 1732, 1479, 1457, 1417, 1367, 1317, 1254, 1156, 1086, 1064, 1050, 1033, 967, 919, 881, 852, 735, 704, 647, 614 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.45 (s), 1.48 (s), 1.36-2.30 (br m), 2.85 (br m), 3.10 (br m), 3.90 (m), 4.03 (m), 4.60-5.08 (br m); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 20.2, 20.5, 23.4, 23.7, 28.0, 28.1, 42.2, 44.2, 56.9, 82.7, 83.3, 83.6, 152.7, 170.9, 171.5; HRMS (EI) calcd for $C_{15}H_{27}O_6N_2$ $[M+H]^+$ *m/z* 331.1869, found *m/z* 331.1861.

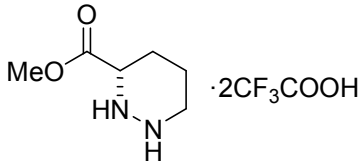


112

(*S*)-1,2-di-*tert*-Butyl 3-Methyl Piperazine-1,2,3-tricarboxylate (112)

To a cooled (0 °C) solution of crude carboxylic acid **40** (1.22 g, 3.70 mmol) in MeOH (20 mL) was added dropwise a solution of $TMSCHN_2$ (2*M* solution in Et_2O, 2.8 mL, 5.56 mmol) at 0 °C and the resulting mixture was allowed to warm to room

temperature with stirring. After 12.5 h, the reaction mixture was quenched with 10% aqueous AcOH (10 mL) and extracted with Et_2O (3 x 30 mL). The organic phase was washed with saturated $NaHCO_3$ (30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (1:7 Et_2O/hexanes 10-40% EtOAc/hexanes) to afford methyl ester **112** (800 mg, 63%) as a colorless oil: $[\alpha]_D^{30}$ -36.4 (*c* 1.00, $CHCl_3$); IR (neat) 2977, 2931, 2856, 1740, 1703, 1478, 1456, 1393, 1367, 1326, 1297, 1252, 1168, 1127, 1086, 1051, 1033, 1007, 952, 910, 880, 857, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.48 (s), 1.49 (s), 1.75 (br m), 1.90 (br m), 2.20 (m), 2.85 (br m), 3.74 (s), 3.95 (br), 4.12 (m), 4.81 (br), 5.01 (br); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 20.0, 24.3, 28.2, 42.7, 51.9, 54.5, 80.2, 81.7, 154.0, 154.6, 170.4; HRMS (CI) calcd for $C_{16}H_{29}N_2O_6$ $[M+H]^+$ *m/z* 345.2026, found *m/z* 345.2014.

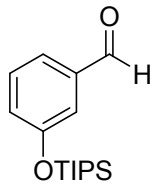


113

(*S*)-Methyl Piperazine-3-carboxylate (113)

To a stirred solution of methyl ester **112** (776 mg, 2.25 mmol) in DCM (7.5 mL) at 0 °C was added TFA (7.5 mL) over 1 min and the resulting mixture was allowed to warm to room temperature with stirring for 1 h. The mixture was concentrated *in vacuo* and the oily residue was azeotroped with toluene to remove

residual traces of acid. This gave crude TFA salt **113** (743 mg, 89%) as a yellow oil: $[\alpha]_D^{23}$ +2.5 (*c* 1.00, $CHCl_3$); IR (neat) 3420, 3259, 2960, 2922, 2851, 2747, 1734, 1682, 1444, 1204, 1139, 840, 801, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.94-2.01 (m, 3H), 2.18-2.21 (m, 1H), 3.30-3.40 (m, 2H), 3.82 (s, 3H), 3.99-4.02 (m, 1H), 6.20 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 19.7, 24.7, 45.1, 52.8, 55.8, 171.4; HRMS (CI) calcd for $C_6H_{11}N_2O_2$ $[M-H]^+$ *m/z* 143.0821, found *m/z* 143.0813. The TFA salt was used in the next step without purification.

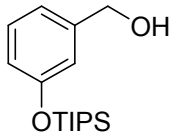


326

3-(Triisopropylsilyloxy)benzaldehyde (326)

To a stirred solution of 3-hydroxybenzaldehyde (**325**) (1.12 g, 9.89 mmol) and imidazole (2.02 g, 29.66 mmol) in DMF (33 mL) at -50 °C was added dropwise TIPSOTf (4.54 g, 14.83 mmol) and the resulting mixture was allowed to warm to room temperature with stirring. After 10 h, the reaction mixture was partitioned between EtOAc (60 mL) and water (24 mL) and the aqueous layer was extracted with EtOAc-hexanes (1:1, 3 x 48 mL). The combined organic extracts were washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent *in vacuo* afforded the crude product which was purified by flash chromatography (10% Et_2O/hexanes) to provide ether **326** (3.05 g, quant.) as a colorless oil: IR (neat) 2945, 2889, 2868, 2723,

1705, 1598, 1583, 1483, 1446, 1387, 1279, 1167, 1146, 1073, 1003, 968, 920, 882, 829, 789, 733, 683, 644 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.13 (d, *J* = 7.2 Hz, 18H), 1.34-1.27 (m, 3H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.39-7.42 (m, 2H), 7.46-7.48 (d, *J* = 7.6 Hz, 1H), 9.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.6, 17.9, 119.6, 123.2, 126.3, 130.0, 138.0, 156.8, 192.0.

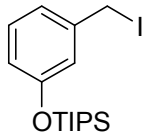


327

(3-(Triisopropylsilyloxy)phenyl)methanol (327)

To a stirred solution of aldehyde **326** (2.87 g, 10.31 mmol) in MeOH (50 mL) at room temperature was added $NaBH_4$ (585 mg, 15.46 mmol) and the resulting suspension was stirred for 40 min. The reaction mixture was concentrated, the residue was quenched with H_2O (30 mL) and the mixture was extracted with EtOAc (3 x 50 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo* to give crude alcohol **327** (2.87 g, 99%) as a colorless oil: IR (neat) 3331 (br), 2945, 2892, 2867, 1604, 1587, 1486, 1464, 1444, 1385, 1367, 1281, 1166, 1004, 958, 920, 883, 821, 782, 689 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.13 (d, *J* = 7.6 Hz, 18H), 1.26-1.33 (m, 3H), 2.00 (br s, 1H), 4.66 (s, 2H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.92-6.95 (m, 2H), 7.22 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 17.9, 65.2, 118.4, 119.0, 119.4,

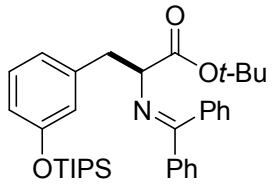
129.5, 142.5, 156.3; HRMS (CI) calcd for $C_{16}H_{28}O_2Si$ $[M]^+$ *m/z* 280.1859, found *m/z* 280.1851. The crude alcohol was used in the next step without purification.



328

(3-(Iodomethyl)phenoxy)triisopropylsilane (328)

To a stirred solution of PPh_3 (561 mg, 2.14 mmol) and imidazole (146 mg, 2.14 mmol) in DCM (10 mL) at room temperature was added I_2 (543 mg, 2.14 mmol). After 15 min, a solution of alcohol **327** (500 mg, 1.78 mmol) in DCM (5 mL) was added dropwise to the reaction mixture and stirring was continued for 30 min. The resulting suspension was passed through a short column of silica and eluted with DCM. The DCM eluate was shaken with saturated aqueous $Na_2S_2O_3$ (15 mL), dried over anhydrous $MgSO_4$, filtered and concentrated to provide crude iodide **328** (669 mg, 96 %) as a pale yellow oil: IR (neat) 2944, 2891, 2866, 1602, 1584, 1484, 1464, 1440, 1385, 1282, 1173, 1156, 1072, 1003, 978, 920, 882, 817, 782, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.13 (d, *J* = 7.2 Hz, 18H), 1.23-1.32 (m, 3H), 4.42 (s, 2H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 5.5, 12.7, 17.9, 119.5, 120.4, 121.3, 129.6, 140.6, 156.2; HRMS (EI) calcd for $C_{16}H_{27}IOSi$ $[M]^+$ *m/z* 390.0876, found *m/z* 390.0873. The iodide was used in the next step without further purification.

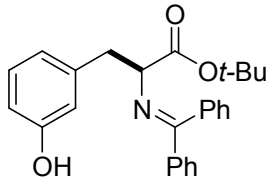


331

(*S*)-*tert*-Butyl 2-(Diphenylmethyleneamino)-3-(3-(triisopropylsilyloxy)phenyl) propanoate (331)

To a stirred solution of iodide **328** (2.50 g, 6.40 mmol), imino ester **329** (1.89 g, 6.40 mmol), and catalyst **330** (556 mg, 1.02 mmol) in a mixture of DCM (25 mL) and toluene (50 mL) at -10 °C was added a 50% aqueous KOH solution (50 mL) and the resulting mixture was stirred vigorously at -5 °C for 33 h. Heptane (65 mL) and water (65 mL) were added to the mixture and the aqueous layer was extracted with heptane (2 x 100 mL). The combined organic phases were washed with H_2O (200 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford the crude product which was purified by flash chromatography (10% EtOAc in hexanes with 1% Et_3N) to furnish ester **331** (2.92 g, 82%) as a viscous orange oil: $[\alpha]_D^{22}$ -110.6 (*c* 1.00, $CHCl_3$); IR (neat) 3059, 3020, 2944, 2892, 2867, 1735, 1624, 1601, 1585, 1485, 1463, 1445, 1391, 1368, 1272, 1152, 1073, 1030, 1004, 980, 910, 883, 850, 805, 780, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.05 (d, *J* = 7.2 Hz, 18H), 1.13-1.19 (m, 3H), 1.47 (s, 9H), 3.12 (dd, *J* = 9.2, 13.2 Hz, 1H), 3.23 (dd, *J* = 4.4, 13.2 Hz, 1H), 4.14 (dd, *J* = 4.4, 9.2 Hz, 1H), 6.64-6.75 (m, 5H), 7.07 (t, *J* = 8.0 Hz, 1H), 7.29-7.41 (m, 6H), 7.63 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.6, 17.9, 28.1,

39.6, 67.9, 81.0, 117.6, 121.4, 122.5, 127.8, 127.9, 128.1, 128.2, 128.8, 128.9, 130.0, 136.5, 139.6, 139.9, 155.8, 170.2, 170.8; HRMS (ES) calcd for $C_{35}H_{48}NO_3Si$ $[M+H]^+$ *m/z* 558.3403, found *m/z* 558.3384.

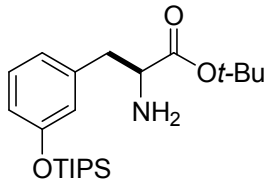


332

(*S*)-*tert*-Butyl 2-(Diphenylmethyleneamino)-3-(3-hydroxyphenyl)propanoate (332)

To a stirred solution of TIPS ether **331** (50.0 mg, 0.0896 mmol) in THF (0.45 mL) at room temperature was added TBAF (1*M* solution in THF, 0.11 mL, 0.110 mmol) and the resulting solution was stirred at room temperature for 4 h. The reaction mixture was quenched with H_2O (0.50 mL) and the aqueous phase was extracted with ether (3 x 0.50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the residue by flash chromatography (10% to 30% EtOAc in hexanes) furnished phenol **332** (34.2 mg, 95%) as a colorless oil: $[\alpha]_D^{25}$ -137.6 (*c* 1.00, $CHCl_3$); IR (neat) 3414, 3059, 2977, 2928, 1729, 1602, 1589, 1488, 1454, 1393, 1369, 1275, 1152, 1076, 1029, 1000, 978, 934, 911, 876, 845, 780, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.46 (s, 9H), 3.12 (dd, *J* = 9.2, 13.2 Hz, 1H), 3.20 (dd, *J* = 4.4, 13.2 Hz, 1H), 4.15 (dd, *J* = 4.4, 9.2 Hz, 1H), 5.48 (br s, 1H), 6.55 (s, 1H), 6.62-6.71 (m, 4H), 7.06 (t, *J* = 8.0 Hz, 1H), 7.28-7.37 (m, 6H), 7.59 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 28.1,

39.4, 67.8, 81.4, 113.3, 116.8, 122.1, 127.7, 128.0, 128.1, 128.4, 128.8, 129.3, 130.2, 136.3, 139.5, 140.0, 155.6, 170.8, 170.9; HRMS (ES) calcd for $C_{26}H_{28}NO_3$ $[M+H]^+$ *m/z* 402.2069, found *m/z* 402.2055.

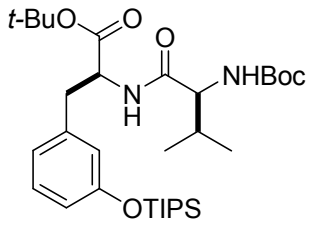


244

(*S*)-*tert*-Butyl 2-Amino-3-(3-(triisopropylsilyloxy)phenyl)propanoate (244)

To a stirred mixture of imine **331** (302 mg, 0.542) in THF (1.1 mL) and H_2O (1.1 mL) at room temperature was added acetic acid (1.1 mL) and the resulting mixture was stirred at room temperature for 6 h. The mixture was diluted with H_2O (3.0 mL) and neutralized with solid Na_2CO3 at 0 °C. The aqueous phase was extracted with EtOAc (3 x 5.0 mL) and the combined organic phases were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (30% EtOAc in hexanes) to afford amino ester **244** (197 mg, 93%) as a yellow oil: $[\alpha]_D^{20}$ +4.5 (*c* 1.00, $CHCl_3$); IR (neat) 2944, 2867, 1732, 1603, 1584, 1486, 1464, 1445, 1391, 1367, 1277, 1156, 1005, 883, 837, 782, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.12 (d, *J* = 7.6 Hz, 18H), 1.24-1.32 (m, 3H), 1.47 (s, 9H), 1.55 (br s, 2H), 2.80 (dd, *J* = 7.6, 13.6 Hz, 1H), 3.02 (dd, *J* = 5.2, 13.6 Hz, 1H), 3.62 (br s, 1H), 6.77-6.82 (m, 3H), 7.14-7.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 17.9, 28.0, 41.2, 56.3, 81.2, 118.0, 121.1, 122.1,

129.3, 139.1, 156.1, 174.2; HRMS (ES) calcd for $C_{22}H_{40}NO_3Si$ $[M+H]^+$ *m/z* 394.2777, found *m/z* 394.2748.

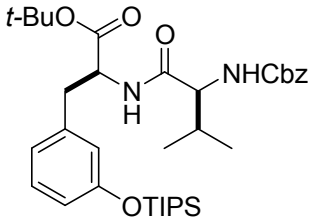


334

(*S*)-*tert*-Butyl 2-((*S*)-2-(*tert*-Butoxycarbonyl)-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoate (334)

To a stirred solution of amino ester **244** (170.9 mg, 0.434 mmol), Boc-Val-OH (**333**) (141.5 mg, 0.651 mmol) and HOBt (167.2 mg, 1.237 mmol) in DCM (3.0 mL) at 0 °C was added EDCI (249.7 mg, 1.303 mmol) and the resulting mixture was allowed to warm to room temperature and stirred at that temperature for 3 h. The reaction mixture was quenched with H_2O (3.0 mL) and the two layers were separated. The aqueous phase was extracted with EtOAc (3 x 5 mL) and the combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash chromatography (20% EtOAc in hexanes) afforded dipeptide **334** (221.9 mg, 86%) as a white foam: $[\alpha]_D^{21}$ +19.5 (*c* 1.00, $CHCl_3$); IR (neat) 3316 (br), 2965, 2929, 2868, 1737, 1656, 1604, 1585, 1530, 1487, 1447, 1392, 1367, 1278, 1160, 1005, 920, 883, 844, 784, 737, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.90 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 1.12 (d, *J* = 7.2 Hz, 18H), 1.24-1.31 (m, 3H), 1.41 (s, 9H), 1.47 (s, 9H), 2.11-2.19 (m,

1H), 2.98-3.10 (m, 2H), 3.95 (br s, 1H), 4.70-4.75 (m, 1H), 5.04 (br s, 1H), 6.29 (br s, 1H), 6.74-6.77 (m, 3H), 7.12-7.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 17.9, 19.2, 27.9, 28.3, 31.0, 38.1, 53.5, 59.8, 82.3, 118.2, 121.1, 122.2, 129.2, 137.5, 156.1, 170.3, 170.9; HRMS (ES) calcd for $C_{32}H_{56}N_2O_6NaSi$ $[M+Na]^+$ *m/z* 615.3805, found *m/z* 615.3809.

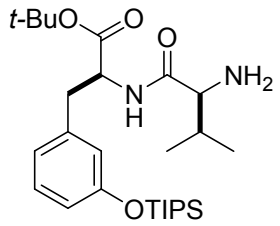


337

(*S*)-*tert*-Butyl 2-((*S*)-2-(Benzyloxycarbonyl)-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoate (337)

To a stirred solution of carbobenzyloxy-L-valine (**336**) (597 mg, 2.375 mmol) and HATU (903 mg, 2.375 mmol) in DMF (14 mL) at room temperature was added DIPEA (1.24 mL, 7.126 mmol) and the resulting mixture was stirred for 5 min, at which point a solution of amino ester **244** (850 mg, 2.159 mmol) in DMF (14 mL) was added. The reaction was stirred for 45 min and diluted with EtOAc (30 mL). The mixture was washed with H_2O (30 mL) and brine (30 mL), then dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography (10% EtOAc/hexanes) to provide dipeptide **337** (1.258 g, 93%) as a white foam: $[\alpha]_D^{20}$ +20.1 (*c* 1.00, $CHCl_3$); IR (neat) 3309 (br), 2965, 2944, 2868, 1732, 1657, 1604, 1585, 1537, 1486, 1455, 1392, 1368, 1279, 1246, 1159, 1105, 1028,

1005, 919, 883, 833, 784, 735, 695, 661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.91 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 7.2 Hz, 18H), 1.22-1.28 (m, 3H), 1.41 (s, 9H), 2.11-2.16 (m, 1H), 3.00-3.05 (m, 2H), 4.02-4.04 (m, 1H), 4.70-4.75 (m, 1H), 5.12 (s, 2H), 5.39 (d, *J* = 8.4 Hz, 1H), 6.29 (d, *J* = 8.0 Hz, 1H), 6.72-6.76 (m, 3H), 7.11 (t, *J* = 8.4 Hz, 1H), 7.32-7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 17.6, 17.9, 19.1, 27.9, 29.7, 31.2, 38.0, 53.6, 60.2, 67.0, 82.4, 118.2, 121.1, 122.2, 128.0, 128.1, 128.5, 129.3, 136.4, 137.4, 156.1, 156.2, 170.3, 170.5; HRMS (CI) calcd for $C_{35}H_{55}O_6N_2Si$ $[M+H]^+$ *m/z* 627.3829, found *m/z* 627.3852.

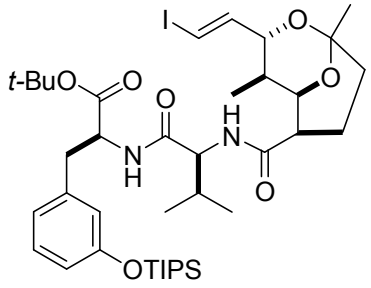


338

(*S*)-*tert*-Butyl 2-((*S*)-2-Amino-3-methylbutanamido)-3-(3-(triisopropylsilyloxy) phenyl)propanoate (338)

A mixture of dipeptide **337** (28 mg, 0.045 mmol) and Pd/C (10%, 3.5 mg) in EtOH at room temperature was stirred under H_2 gas (1 atm) for 19 h. The suspension was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (50% EtOAc/hexanes) to give dipeptide **338** (18.4 mg, 84%) as a colorless oil: $[\alpha]_D^{21}$ +12.1 (*c* 1.00, $CHCl_3$); IR (neat) 3369 (br), 3002 (br), 2968, 2920, 2831, 1731, 1652, 1600, 1582, 1539, 1481, 1390, 1366, 1240, 1149,

1101, 1023, 918, 883, 834, 789, 730, 691, 659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.75 (d, *J* = 6.8 Hz, 3H), 0.954 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 18H), 1.20-1.30 (m, 3H), 1.39 (s, 9H), 2.24-2.25 (m, 1H), 3.03 (d, *J* = 6.4 Hz, 2H), 3.21-3.22 (m, 1H), 4.72-4.77 (m, 1H), 6.73-6.77 (m, 3H), 7.10-7.14 (m, 1H), 7.66-7.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 16.1, 17.9, 19.7, 28.0, 30.8, 38.3, 53.1, 60.2, 82.0, 118.0, 121.1, 122.1, 129.1, 137.9, 156.0, 170.9, 174.0; HRMS (CI) calcd for $C_{27}H_{49}O_4N_2Si$ $[M+H]^+$ *m/z* 493.2257, found *m/z* 493.2284.

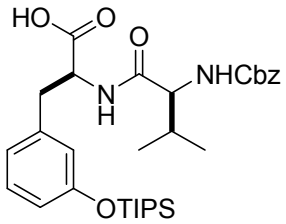


339

(*S*)-*tert*-Butyl 2-((*S*)-2-((3*R*,4*R*,5*R*,6*R*)-3-((*E*)-2-iodovinyl)-1,4-dimethyl-2,9-dioxa-bicyclo[3.3.1]nonane-6-carboxamido)-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoate (339)

To a stirred solution of iodo acid **242** (6.0 mg, 0.0170 mmol) and HATU (7.1 mg, 0.0187 mmol) in DMF (0.68 mL) at room temperature was added DIPEA (10 μL, 0.0562 mmol) and the resulting mixture was stirred for 5 min, at which point a solution of dipeptide **338** (9.2 mg, 0.0187 mmol) in DMF (0.38 mL) was added. The solution was stirred for 1.5 h and diluted with EtOAc (1.0 mL). The mixture was washed with H_2O (1.0 mL) and brine (1.0 mL), dried over anhydrous $MgSO_4$, filtered

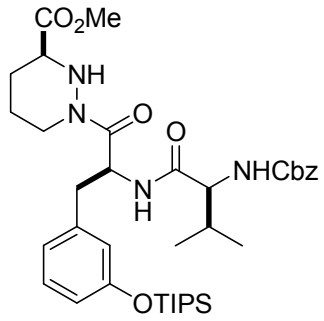
and concentrated under reduced pressure. The crude product was purified by flash chromatography (25% EtOAc/hexanes) to provide ester **339** (11.4 mg, 81%) as a colorless oil: $[\alpha]_D^{20}$ +6.2 (*c* 0.85, $CHCl_3$); IR (neat) 3284, 3069, 2961, 2942, 2929, 2867, 2896, 1737, 1639, 1605, 1585, 1549, 1486, 1463, 1448, 1385, 1368, 1279, 1157, 1005, 952, 883, 846, 837, 781, 734, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.85 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 7.2 Hz, 18H), 1.20-1.30 (m, 6H), 1.42 (s, 9H), 1.85-1.98 (m, 2H), 2.00-2.21 (m, 4H), 2.62-2.63 (m, 1H), 3.01-3.07 (m, 2H), 4.24-4.31 (m, 2H), 4.41-4.44 (m, 1H), 4.68-4.77 (m, 1H), 6.14 (d, *J* = 7.6 Hz, 1H), 6.47 (s, 1H), 6.48 (s, 1H), 6.73-6.79 (m, 3H), 7.11-7.15 (m, 1H), 7.40 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.6, 17.9, 19.3, 22.8, 27.9, 29.6, 30.9, 31.0, 36.2, 38.0, 38.8, 53.5, 58.1, 71.9, 77.2, 78.8, 79.9, 82.4, 95.7, 118.2, 121.1, 122.1, 129.3, 137.4, 145.3, 156.2, 170.3, 170.5, 174.4; HRMS (ES) calcd for $C_{39}H_{64}N_2O_7ISi$ $[M+H]^+$ *m/z* 827.3528, found *m/z* 827.3552.



342

(*S*)-2-((*S*)-2-(Benzyloxycarbonyl)-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoic Acid (342)

To a solution of *tert*-butyl ester **337** (10.0 mg, 0.0160 mmol) and thioanisole (0.04 mL, 0.340 mmol) in DCM (0.40 mL) at 0 °C was added TFA (0.04 mL, 0.522 mmol) and the resulting mixture was allowed to warm to room temperature with stirring. After 5 h, another portion of TFA (0.30 mL) was added to the reaction mixture (TLC showed that starting material remained), the mixture was stirred for a further 4 h, and was then concentrated under reduced pressure. The residue was purified by flash chromatography (30% EtOAc in hexanes) to furnish carboxylic acid **342** (7.0 mg, 77%) as a white solid: mp. 120-122 °C; $[\alpha]_D^{20}$ +73.6 (*c* 3.71, $CHCl_3$); IR (film) 3310, 3066, 3035, 2961, 2945, 2867, 1717, 1653, 1603, 1585, 1540, 1487, 1446, 1279, 1248, 1162, 1004, 883, 831, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.86 (d, *J* = 6.1 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 18H), 1.21-1.30 (m, 3H), 2.04-2.10 (m, 1H) 3.05-3.06 (m, 1H), 3.12-3.15 (m, 1H), 4.02-4.09 (m, 1H), 4.80-4.83 (m, 1H), 5.07-5.15 (AB quartet, 2H), 5.56 (br s, 1H), 6.54 (br s, 1H), 6.74-6.76 (m, 3H), 7.10 (t, *J* = 7.9 Hz, 1H), 7.30-7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 17.7, 17.9, 19.0, 30.3, 31.0, 37.3, 53.2, 60.4, 60.5, 67.2, 118.7, 120.8, 122.0, 128.0, 128.2, 128.5, 129.5, 137.2, 156.3, 156.5, 171.5, 174.5; HRMS (CI) calcd for $C_{31}H_{47}N_2O_6Si$ $[M+H]^+$ *m/z* 571.3203, found *m/z* 571.3220.

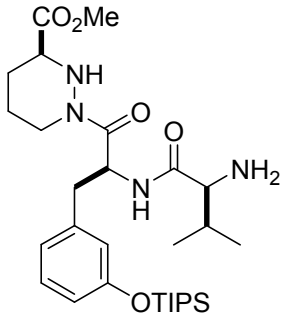


343

(*S*)-Methyl 1-((*S*)-2-((*S*)-2-(Benzyloxycarbonyl)-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoyl)piperazine-3-carboxylate (343)

To a solution of carboxylic acid **342** (4.5 mg, 7.9 μmol) in DMF (0.10 mL) at room temperature was added HATU (3.6 mg, 9.5 μmol) and DIPEA (4.9 μL, 28.4 μmol) and the reaction mixture was stirred for 5 min, at which point piperazic methyl ester **113** (2.9 mg, 7.9 μmol) in DMF (0.10 mL) was added. The resulting mixture was stirred for 2 h, diluted with EtOAc (2 mL), and washed with brine (2 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (20%-40% EtOAc in hexanes) to give tripeptide **343** (4.5 mg, 82%) as a colorless oil: $[\alpha]_D^{20}$ -25.4 (*c* 1.00, $CHCl_3$); IR (neat) 3302, 3066, 3032, 2945, 2867, 1745, 1642, 1537, 1486, 1442, 1271, 1236, 1164, 1004, 983, 883, 834, 757, 695; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.81 and 0.96 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 7.2 Hz, 18H), 1.22-1.28 (m, 3H), 1.42-1.51 (m, 2H), 1.61-1.86 (m, 3H), 2.02-2.18 (m, 1H), 2.50-2.61 (m, 1H), 2.83-2.96 (m, 2H), 3.23 and 3.47 (d, *J* = 11.0 Hz, 1H), 3.72 and 3.76 (s, 3H),

4.03-4.08 (m, 1H), 4.03-4.08 and 4.48-4.52 (m, 1H), 5.10-5.17 (m, 2H), 5.38 (br s, 1H), 5.61-5.66 and 5.73-5.78 (m, 1H), 6.51 (m, 1H), 6.67-6.79 (m, 3H), 7.09-7.14 (m, 1H), 7.32-7.39 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 17.3 and 17.5, 17.9, 19.2, 22.4 and 22.9, 28.2 and 28.7, 31.4 and 31.7, 39.1 and 39.5, 41.9 and 42.0, 49.7 and 50.0, 52.1, 57.7 and 58.4, 60.0 and 60.2, 67.0, 118.1, 121.0 and 121.4, 122.2 and 122.4, 128.1, 128.5, 129.1 and 129.2, 136.4, 138.0, 156.0, 156.1, 156.3, 170.2 and 170.4, 171.5 and 171.7, 172.3; HRMS (ES) calcd for $C_{37}H_{57}N_4O_7Si$ $[M+H]^+$ *m/z* 697.3997, found *m/z* 697.3976.



241

(*S*)-Methyl 1-((*S*)-2-((*S*)-2-Amino-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoyl)piperazine-3-carboxylate (241)

A suspension of tripeptide **343** (164 mg, 0.236 mmol) and 10% Pd/C in ethanol (12.0 mL) was stirred under an atmosphere of H_2 (1 atm) for 19 h. The catalyst was removed by filtration and the filtrate was evaporated. The crude product was purified by flash chromatography (10% MeOH in DCM + 1% Et_3N) to afford tripeptide **241** (131 mg, 99%) as a yellow oil: $[\alpha]_D^{20}$ -21.5 (*c* 1.00, $CHCl_3$); IR (neat)

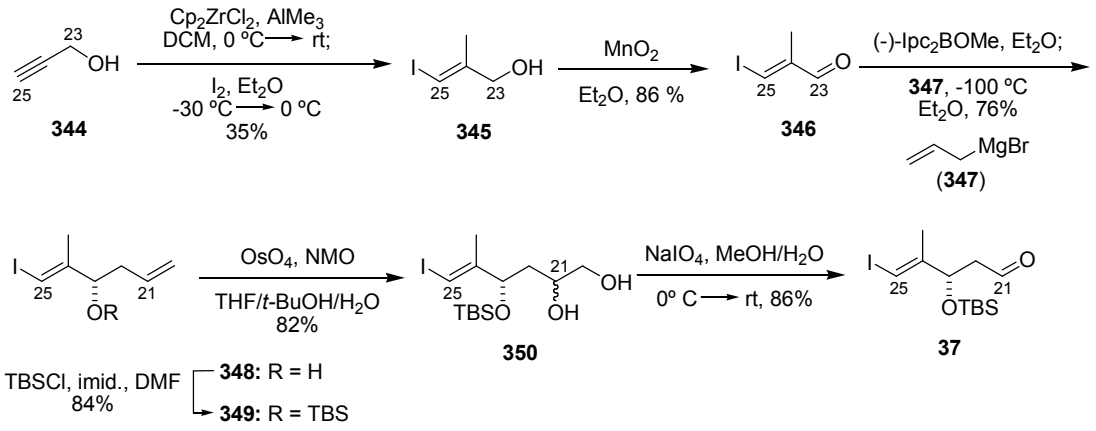
3336, 3245, 2925, 2867, 1746, 1652, 1603, 1585, 1486, 1443, 1273, 1164, 1004, 982, 883, 834, 688, 662 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.84-1.00 (m, 6H), 1.10 (d, *J* = 7.2 Hz, 18H), 1.21-1.29 (m, 3H), 1.40-1.80 (m, 4H), 2.01-2.30 (m, 3H), 2.70-2.95 (m, 3H), 3.50 (br s, 1H), 3.60-3.70 (m, 6H), 4.20-4.30 (m, 1H), 5.65-5.72 (m, 1H), 6.69-6.90 (m, 3H), 7.05-7.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.7, 14.1, 17.1, 17.5, 17.9, 19.2, 22.7, 28.2, 29.7, 29.7, 30.6, 30.8, 38.0, 39.0, 41.7, 49.7, 52.1, 57.9, 59.9, 70.6, 118.0, 120.9, 121.4, 122.4, 129.1, 129.2, 138.3, 138.6, 156.0, 156.1, 171.8, 172.1, 172.5; HRMS (ES) calcd for $C_{29}H_{51}N_4O_5Si$ $[M+H]^+$ *m/z* 563.3629, found *m/z* 563.3615.

CHAPTER 5: STUDIES TOWARDS THE SYNTHESIS OF THE C1-C25 MACROLATONE OF SFA: ASSEMBLY OF TRIPEPTIDE 241, CARBOXYLIC ACID 242 AND VINYL BORONATE 240

Our approach to macrolactone **239** required three subunits, specifically tripeptide **241**, carboxylic acid **242** and vinyl boronate **240**. In this plan, amide bond formation at N12-C13 was programmed to produce C1-C19 segment **357**, which upon esterification with alcohol **240** would provide a C1-O connection. Intramolecular palladium-catalyzed Suzuki-Miyaura cross coupling[1, 2] of **358** would create the C19-C20 linkage leading to mactolactone **239**.

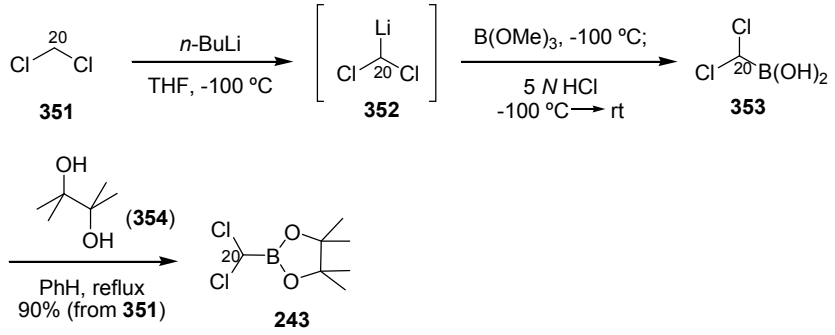
5.1 Synthesis of C20-C25 Vinyl Boronate 240

Synthesis of vinyl boronate **240** comprising C20-C25 of SFA commenced with zirconation-methylation-iodination of propargyl alcohol **344** to give known iodide **345**.[3] Oxidation of this alcohol with manganese dioxide[4] provided aldehyde **346** which was subjected to asymmetric allylboration[5] using allylmagnesium bromide (**347**) to afford homoallylic alcohol **348** (Scheme 5.1). Subsequent protection of the secondary alcohol of **348** with *tert*-butyldimethylsilyl chloride delivered silyl ether **349** which was transformed into diol **350** using a regioselective osmium tetroxide-mediated dihydroxylation in the presence of stoichiometric *N*-methylmorpholine-*N*-oxide. Oxidation of **350** with sodium periodate in methanol-water furnished aldehyde **37**.[6]



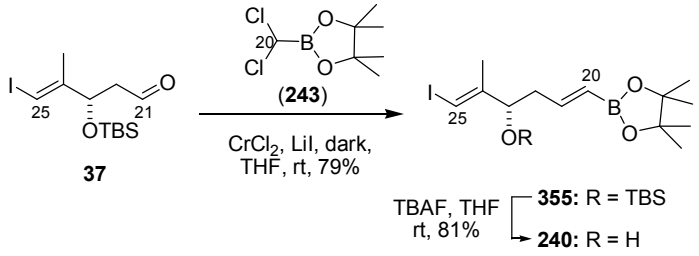
Scheme 5.1 Synthesis of aldehyde **37** (14% yield, *6 steps*)

Our next task was conversion of aldehyde **37** into a vinyl boronate using Takai olefination.[7] This operation required dichloromethylboronate **243** which was prepared from dichloromethane (**351**) by the method of Wuts and Thompson,[8] as shown in Scheme 5.2. Thus, dichloromethane was lithiated with *n*-butyllithium at low temperature to give carbanion **352** which was treated with trimethoxyborane and then with 5*N* hydrochloric acid to deliver dichloromethylboronic acid **353**. Finally, **353** was reacted with pinacol (**354**) in refluxing benzene to afford boronate **243**.



Scheme 5.2 Synthesis of dichloromethylboronate **243** (90% yield, *3 steps*)

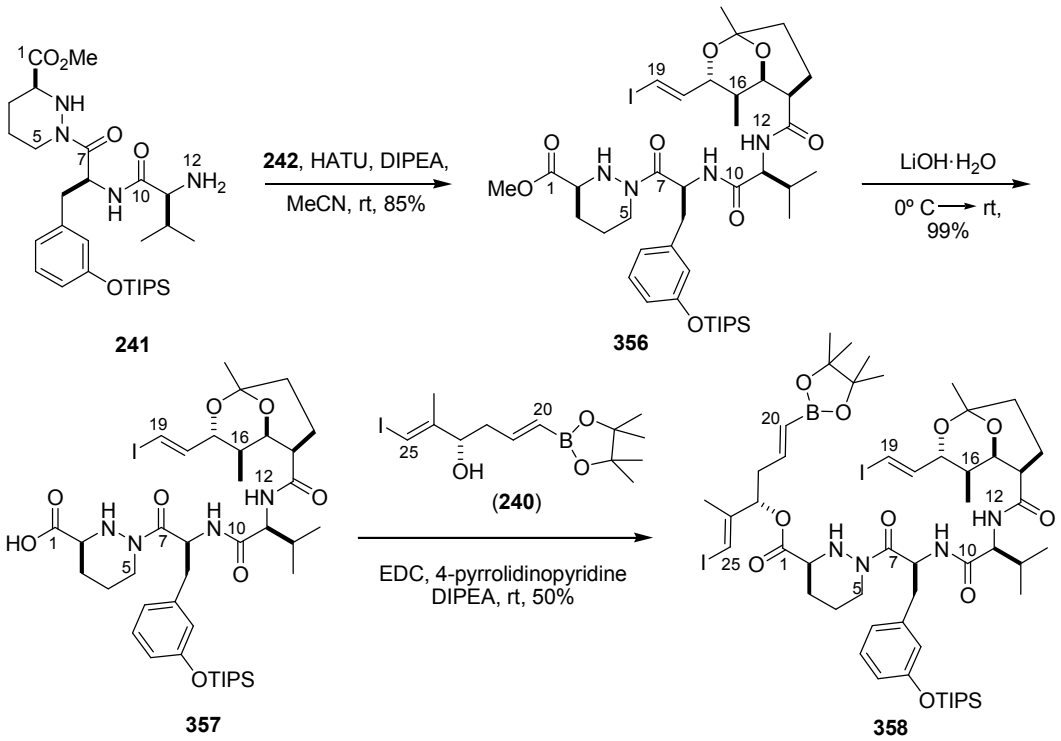
With aldehyde **37** and boronate **243** in hand, the synthesis of vinyl boronate **240** was carried out using Takai's methodology.[7] As shown in Scheme 5.3, aldehyde **37** was treated with boronate **243** in the presence of chromous chloride and lithium iodide to give **355** from which the *tert*-butyldimethylsilyl group was removed with tetra-*n*-butylammonium fluoride to yield alcohol **240**. The synthesis of **240** was completed in 9% overall yield from propargyl alcohol (**344**) in a sequence of eight steps.



Scheme 5.3 Synthesis of vinyl boronate **240** (64% yield, *2 steps*)

5.2 Studies Toward the Synthesis of the C1-C25 Macrolactone 239

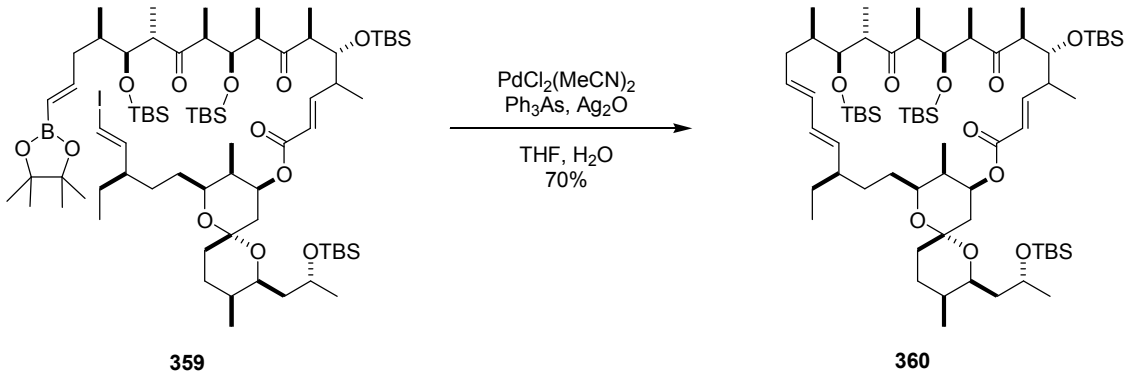
The approach to macrolactone **239** began with acylation of tripeptide **241** with carboxylic acid **242** in the presence of *N,N,N′,N′*-tetramethyl-*O*-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate and Hunig's base in acetonitrile. This led to **356**, from which the methyl ester was cleaved with lithium hydroxide to furnish carboxylic acid **357** (Scheme 5.4). This carboxylic acid was esterified with alcohol **240** in the presence of 4-pyrrolidinopyridine, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and diisopropylethylamine to afford macrocyclization precursor **358**.



Scheme 5.4 Synthesis of vinyl iodide **358** (42% yield, *3 steps*)

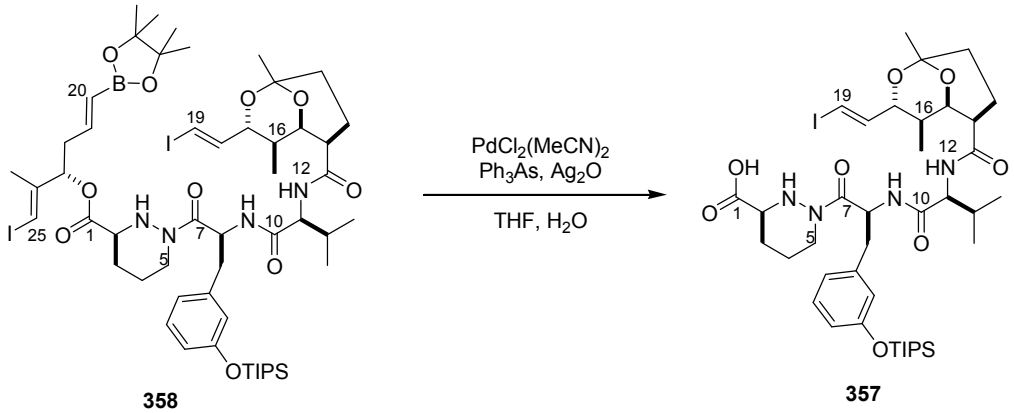
With intramolecular Suzuki-Miyaura coupling[1] envisioned as the key to closing **358** to macrocycle **239**, precedent was sought as a guide in selecting appropriate reaction conditions for this challenging operation. In 1998, White and coworkers[2, 9] utilized an intramolecular Suzuki-Miyaura coupling to complete macrocycle **360** from vinyl boronate **359** in their total synthesis of rutamycin B (Scheme 5.5), and following that precedent **358** was reacted with bis(acetonitrile)dichloropalladium(II) and triphenylarsine in the presence of silver oxide and water. However, no evidence for macrocyclization was found, hydrolysis of the ester bond at C1-O to give **357** being the sole outcome (Scheme 5.6). In the presence of silver(I) oxide (four equivalents) and water, this reaction generates

hydroxide ion and we believe that, in contrast to **359**, saponification of **358** to return **357** and (presumably) **240** takes precedence over intramolecular coupling in this case. The approach to macrolactone **239** ended at this point due to a lack of advanced materials.



359 **360**

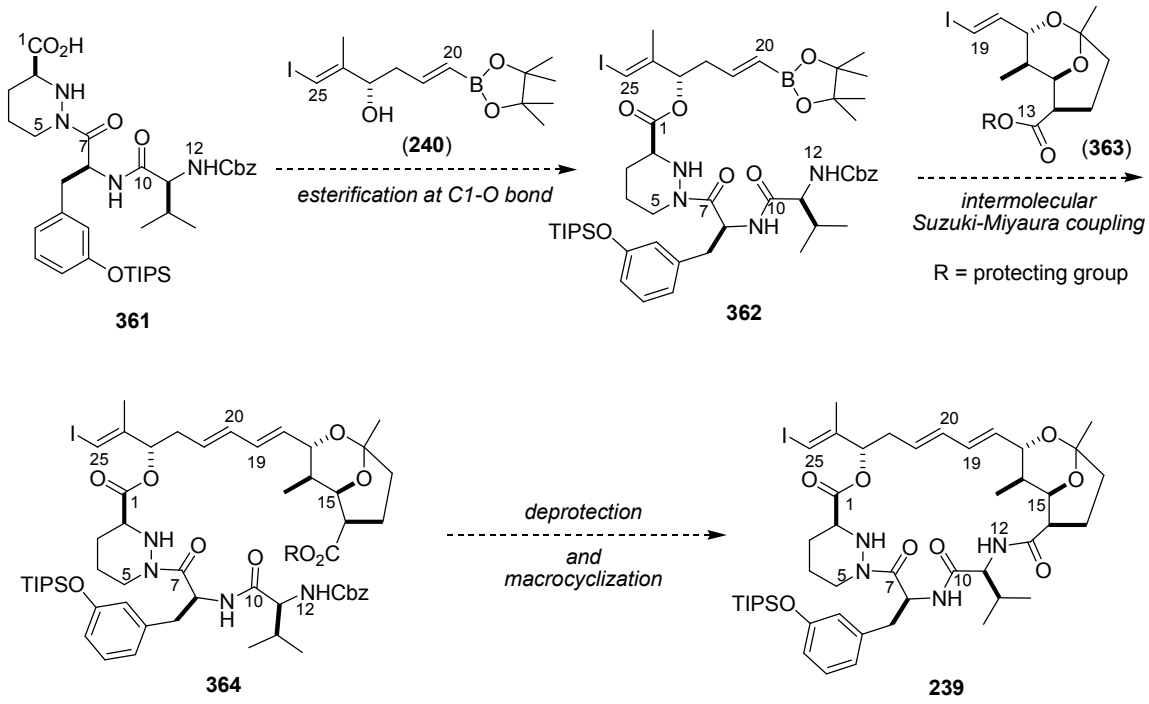
Scheme 5.5 White's synthesis of macrolactone **360** from **359** using intramolecular Suzuki-Miyaura coupling



358 **357**

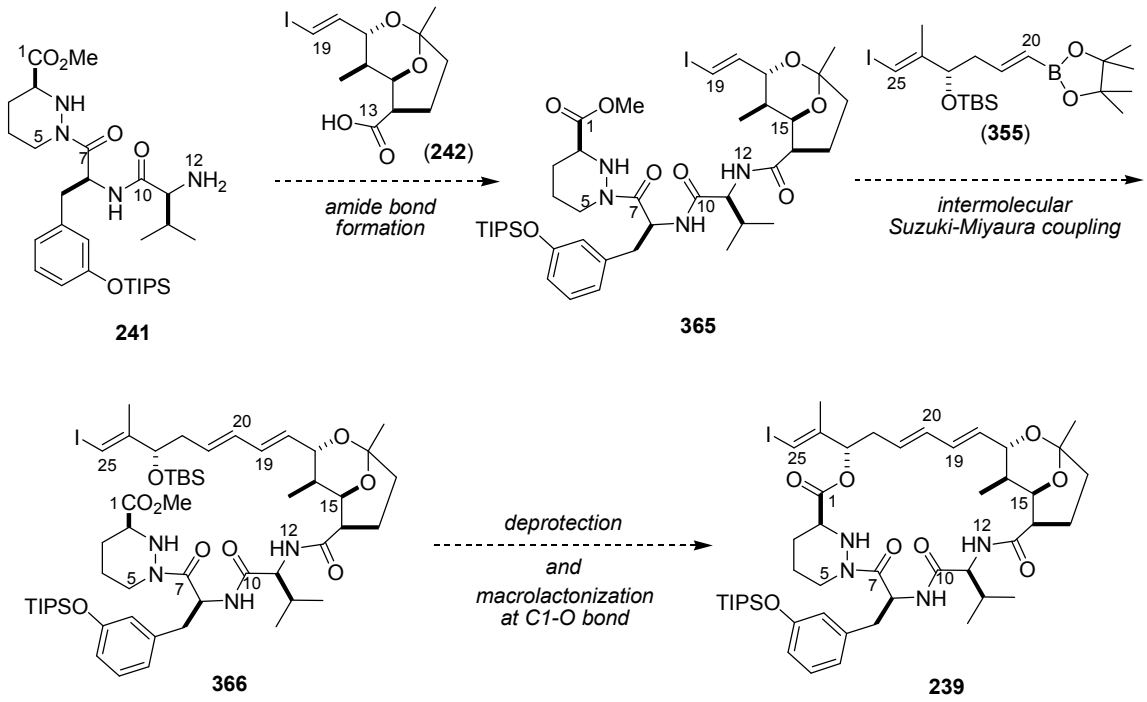
Scheme 5.6 Formation of carboxylic acid **357** under Suzuki-Miyaura conditions

The unsuccessful attempt at intramolecular Suzuki-Miyaura coupling under conditions shown in Scheme 5.6 will require a new strategy for acquiring macrocycle **239**. Shown in Schemes 5.7 and 5.8 are approaches to **239** based on intermolecular Suzuki-Miyaura coupling where the order of assembly of subunits has been changed. In Scheme 5.7, esterification of **361** with **240** is proposed as a route to **362**, after which intermolecular Suzuki-Miyaura coupling of **362** with vinyl iodide **363** would generate amino acid **364**. Protecting groups would be removed from **364** and macrolactamization should then give **239**.



Scheme 5.7 A new approach to macrocycle **239** via intermolecular Suzuki-Miyaura coupling

An alternative strategy for reaching **239** is shown in Scheme 5.8 where amide bond formation between **241** and **242** initiates the sequence. This would lead to vinyl iodide **365** which should undergo intermolecular Suzuki-Miyaura coupling with **355** to produce macrolactone precursor **366**. Removal of protecting groups and macrolactonization at the C1-O bond would be the end game strategy in this pathway to **239**.



241 **(242)** **365** **(355)** **366** **239**

Scheme 5.8 An alternative strategy for synthesis of macrolactone **239**

5.3 References

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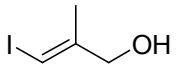
5.4 Experimental Section

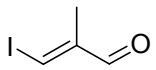


345

(*E*)-3-Iodo-2-methylprop-2-en-1-ol (345)

To a suspension of zirconocene dichloride (652 mg, 2.23 mmol) in DCM (19 mL) at room temperature was added trimethylaluminum (2.57 mL) and the mixture was cooled to 0 °C. A solution of propargyl alcohol (**344**) (500 mg, 8.92 mmol) in DCM (18 mL) was added via cannula and the mixture was allowed to warm to room temperature with stirring for 10 h. The mixture was cooled to -30 °C and a solution of iodine (3.39 g, 13.38 mmol) in Et_2O (5.2 mL) was added. The resulting mixture was stirred at -30 °C for 30 min and allowed to warm to 0 °C. The solution was poured into a mixture of saturated aqueous sodium potassium tartrate (26 mL) and pentane (173 mL) and stirred vigorously for 10 min. The layers were separated and the aqueous phase was extracted with Et_2O (3 x 43 mL). The combined organic extracts were washed with brine (100 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent *in vacuo* gave alcohol **345** (615.1 mg, 35%) as a yellow oil: IR (neat) 3335, 3074, 3047, 2915, 2864, 1732, 1683, 1621, 1446, 1377, 1276, 1253, 1147, 1069, 1013, 942, 883, 832, 776, 704, 667, 576 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.81 (br,

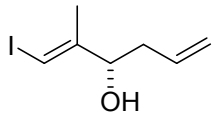
1H), 1.87 (s, 3H), 4.14 (s, 2H), 6.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 21.3, 67.2, 77.3, 147.2.



346

(*E*)-3-Iodo-2-methylacrylaldehyde (346)

To a stirred solution of alcohol **345** (270 mg, 1.52 mmol) in Et_2O (15 mL) was added freshly prepared MnO_2 (1.32 g, 15.15 mmol) and the suspension was stirred vigorously for 10 h. The suspension was filtered and the filtrate was concentrated under reduced pressure to give aldehyde **346** (230 mg, 86%) as a yellow oil: IR (neat) 3527, 3345, 3047, 2954, 2920, 2821, 2722, 1690, 1593, 1375, 1294, 1147, 1013, 831, 799, 695, 633 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.93 (s, 3H), 7.82 (s, 1H), 9.54 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 16.5, 109.5, 150.8, 189.5. The aldehyde was used in the next step without purification.

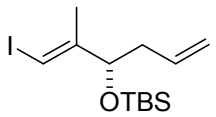


348

(*S*,*E*)-1-Iodo-2-methylhexa-1,5-dien-3-ol (348)

Allylmagnesium bromide (**347**) (3.60 mL, 1*M* solution in ether, 3.60 mmol) was added dropwise to a solution of (−)-$(Ipc)_2$BOMe (1.13 g, 3.58 mmol) in Et_2O (16.0 mL) at 0 °C and the resulting pale gray slurry was allowed to warm to 25 °C over 1 h. The solvent was removed under reduced pressure and pentane (4.0 mL) was

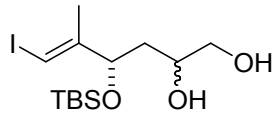
added to the residual solid. The resulting slurry was stirred at 25 °C for 10 min and the solids were allowed to settle over 30 min. The clear supernatant was transferred carefully to a flask via cannula. This process was repeated four times (4.0 mL of pentane each, 16.0 mL total volume) and the resulting solution was added dropwise over 1 h to a solution of aldehyde **346** (540.0 mg, 2.76 mmol) in Et_2O (10 mL) at -100 °C. After 1 h at -100 °C, MeOH (0.2 mL) was added to the solution and the mixture was allowed to warm to room temperature over 40 min. Saturated aqueous $NaHCO_3$ (2.4 mL) and H_2O_2 (2.0 mL of a 30% aqueous solution) were added with stirring over 12 h. The layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with saturated aqueous NH_4Cl (15 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Flash chromatography (silica gel, 20% ether in hexanes) furnished alcohol **348** (497.7 mg, 76%) as a colorless oil: $[\alpha]_D^{20}$ -18.7 (*c* 0.9, $CHCl_3$); IR (neat) 3384, 3069, 2922, 1702, 1641, 1478, 1454, 1386, 1368, 1277, 1040, 995, 914 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.85 (s, 3H), 1.86 (br s, 1H), 2.29-2.43 (m, 2H), 4.24 (dd, *J* = 5.2, 7.6 Hz, 1H), 5.16 (s, 1H), 5.19 (d, *J* = 3.2 Hz, 1H), 5.71-5.82 (m, 1H), 6.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 20.2, 39.9, 75.4, 78.4, 118.7, 133.6, 149.0; HRMS (CI) calcd for $C_7H_{11}IO$ $[M]^+$ *m/z* 237.9855, found *m/z* 237.9867.



349

(*S*,*E*)-*tert*-Butyl(1-iodo-2-methylhexa-1,5-dien-3-yloxy)dimethylsilane (349)

To a stirred solution of alcohol **348** (138 mg, 0.581 mmol) in DMF (2.0 mL) at 0 °C was added imidazole (111 mg, 1.627 mmol) followed by TBSCl (149 mg, 0.988 mmol) and the resulting mixture was stirred at room temperature for 7 h. The reaction mixture was diluted with Et_2O (2.5 mL) and quenched with saturated aqueous NH_4Cl (2.5 mL). The aqueous phase was extracted with Et_2O (2.5 mL) and the combined organic phases were washed with water (5.0 mL) and brine (5.0 mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give the crude product which was purified by flash chromatography (5% Et_2O/hexanes) to provide silyl ether **349** (172 mg, 84%) as a colorless oil: $[\alpha]_D^{20}$ -16.5 (*c* 1.00, $CHCl_3$); IR (neat) 3078, 2955, 2929, 2900, 2857, 1641, 1615, 1472, 1278, 1253, 1082, 1005, 939, 914, 836, 776, 676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.01 (s, 3H), 0.05 (s, 3H), 0.90 (s, 9H), 1.79 (s, 3H), 2.21-2.34 (m, 2H), 4.18 (t, *J* = 6.4 Hz, 1H), 5.03 (s, 1H), 5.07 (d, *J* = 5.2 Hz, 1H), 5.67-5.77 (m, 1H), 6.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.0, -4.9, 18.2, 19.7, 25.8, 41.0, 77.2, 77.6, 117.1, 134.4, 149.9; HRMS (CI) calcd for $C_{13}H_{25}IOSi$ $[M]^+$ *m/z* 352.0719, found *m/z* 352.0745.

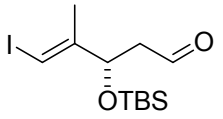


350

(*S*,*E*)-4-(*tert*-Butyldimethylsilyloxy)-6-iodo-5-methylhex-5-ene-1,2-diol (350)

To a solution of olefin **349** (28.9 mg, 85.2 μmol) in a mixture of THF (0.39 mL), *tert*-BuOH (0.39 mL) and H_2O (0.08 mL) at 0 °C was added 4-

methylmorpholine *N*-oxide (NMO) (12.7 mg, 93.7 μmol) followed by OsO_4 (0.10 mL, 0.05*M* in *t*BuOH, 4.26 μmol, 0.05 equiv). The mixture was stirred vigorously at room temperature for 15 h and quenched with saturated aqueous Na_2SO_3 (0.24 mL). The resulting mixture was stirred for 2 h and partitioned between EtOAc (0.30 mL) and water (0.30 mL). The organic phase was separated and the aqueous phase was extracted with EtOAc (2 x 0.40 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered, and the solvents were removed under reduced pressure. Flash chromatography of the residue (50% Et_2O/hexanes) furnished an inseparable 1:1 mixture of diols **350** (25.9 mg, 82%) as a colorless oil: IR (neat) 3329 (br), 3063, 2956, 2928, 1638, 1611, 1469, 1274, 1250, 1087, 1001, 928, 914, 836, 776, 676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.40 and 0.52 (s, 3H), 0.11 and 0.12 (s, 3H), 0.92 (s, 9H), 1.65-1.68 (m, 2H), 1.80 and 1.81 (s, 3H), 3.43-3.52 (m, 1H), 3.60-3.62 (m, 1H), 3.83-3.88 (m, 1H), 4.46-4.52 (m, 1H), 6.30 and 6.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.4 and -5.3, -5.0 and -4.7, 18.0 and 18.1, 19.4 and 20.7, 25.8, 38.2 and 38.9, 66.7 and 67.0, 68.7 and 70.7, 74.9, 78.0 and 78.8, 149.2 and 149.7; HRMS (CI) calcd for $C_{13}H_{27}IO_3Si$ $[M]^+$ *m/z* 386.0774, found *m/z* 386.0734.

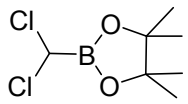


37

(*S*,*E*)-3-(*tert*-Butyldimethylsilyloxy)-5-iodo-4-methylpent-4-enal (37)

Diols **350** (20.0 mg, 0.052 mmol) were dissolved in a mixture of MeOH (0.35 mL) and water (0.17 mL) and the solution was cooled to 0 °C. $NaIO_4$ (66.4 mg, 0.311

mmol) was added portionwise over 5 min, and the resulting slurry was vigorously stirred for 40 min at 25 °C. The mixture was partitioned between DCM (0.5 mL) and water (0.5 mL) and the organic phase was separated. The aqueous layer was extracted with DCM (0.5 mL) and the combined organic extracts were washed with brine (1 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Flash column chromatography (silica gel, 20% Et_2O in hexanes) provided aldehyde **37** (15.7 mg, 86%) as a yellow oil: $[\alpha]_D^{20}$ -29.8 (*c* 1.00, $CHCl_3$); IR (neat) 2954, 2929, 2857, 2719, 1728, 1618, 1472, 1362, 1279, 1255, 1095, 994, 838, 777, 677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.03 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.83 (d, *J* = 0.8 Hz, 3H), 2.47 (ddd, *J* = 2.0, 4.4, 16.0 Hz, 1H), 2.71 (ddd, *J* = 2.8, 8.0, 16.0 Hz, 1H), 4.72 (dd, *J* = 4.0, 8.0 Hz, 1H), 6.37 (d, *J* = 1.2 Hz, 1H), 9.76 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.3, -4.9, 18.1, 19.7, 25.6, 49.7, 72.6, 78.9, 148.8, 200.5; HRMS (CI) calcd for $C_{12}H_{23}IO_2Si$ $[M]^+$ *m/z* 354.0512, found *m/z* 354.0546.

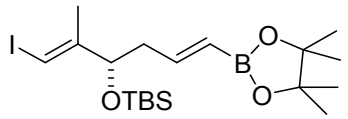


243

2-(Dichloromethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (243)

To a stirred solution of dichloromethane (**351**) (3.73 mL, 55.0 mmol) in THF (100 mL) at -100 °C was added dropwise a solution of *n*-BuLi (31.3 mL, 1.6*M* in hexane, 50.0 mmol) over a period of 40 min and the resulting suspension was stirred for an additional 30 min. Trimethyl borate (6.25 mL, 55.0 mmol) was added in one portion, and after being stirred for 30 min, the reaction mixture was hydrolyzed with

5*N* HCl (10 mL). The mixture was allowed to warm to room temperature and the organic layer was separated. The aqueous layer was extracted with Et_2O (2 x 25 mL) and the combined organic phases were concentrated under reduced pressure to afford crude dichloromethylboronic acid **(353**) as a viscous reddish-brown oil. The crude product was dissolved in benzene (110 mL) and pinacol (**354**) (6.50 g, 55.0 mmol) was added in one portion. The biphasic mixture was heated at reflux under an argon atmosphere for 48 h, utilizing a Dean-Stark trap to remove water, and was then cooled to room temperature. The homogeneous yellow solution was fractionally distilled to afford dichloromethylboronate **243** (9.5 g, 90%) as a colorless oil: bp 103 °C/30 mm Hg; IR (neat) 2982, 2935, 1471, 1408, 1363, 1274, 1214, 1169, 1137, 1111, 1007, 968, 901, 846, 823, 739, 672, 650, 576 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.35 (s, 12H), 5.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 24.5, 85.8.

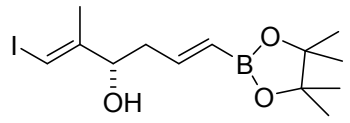


355

***tert*-Butyl((*S*,1*E*,5*E*)-1-iodo-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-1,5-dien-3-yloxy)dimethylsilane (355)**

To a suspension of $CrCl_2$ (27.8 mg, 0.226 mmol) in THF (0.28 mL) at room temperature was added a solution of aldehyde **37** (8.0 mg, 0.023 mmol) and dichloromethyl pinacolboronate (**243**) (11.9 mg, 0.056 mmol) in THF (0.06 mL) followed by dropwise addition of a solution of LiI (15.2 mg, 0.113 mmol) in THF (0.03 mL). The mixture was kept in the dark and was stirred vigorously for 12 h. The

reaction mixture was quenched with ice-cold H_2O (1.0 mL) and extracted with Et_2O (3 x 2.0 mL). The organic phase was washed with brine (2.0 mL), dried over anhydrous $MgSO_4$ and filtered. Removal of the solvent under reduced pressure gave a crude product which was purified by flash chromatography (10% EtOAc in hexanes) to furnish boronate **355** (8.5 mg, 79%) as a colorless oil: $[\alpha]_D^{20}$ -9.6 (*c* 0.50, $CHCl_3$); IR (neat) 2976, 2954, 2928, 2856, 1640, 1363, 1321, 1253, 1146, 1082, 836, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.00 (s, 3H), 0.04 (s, 3H), 0.89 (s, 9H), 1.27 (s, 12H), 1.79 (s, 3H), 2.29-2.42 (m, 2H), 4.22 (t, *J* = 6.0 Hz, 1H), 5.47 (d, *J* = 18.0 Hz, 1H), 6.20 (s, 1H), 6.53 (dt, *J* = 6.8, 18.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.1, -4.9, 18.2, 19.6, 24.7, 25.8, 43.2, 77.2, 77.6, 83.0, 149.9, 150.0; HRMS (ES) calcd for $C_{19}H_{37}BIO_3Si$ $[M+H]^+$ *m/z* 479.1571, found *m/z* 479.1524.

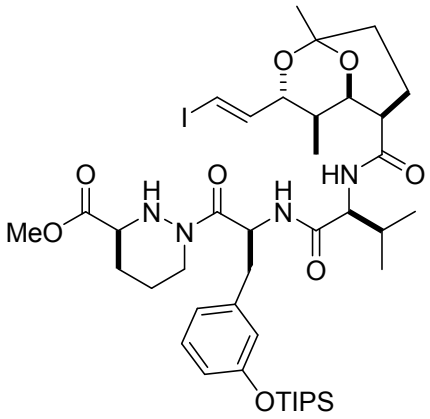


240

(*S*,1*E*,5*E*)-1-Iodo-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-1,5-dien-3-ol (240)

To a stirred solution of boronate **355** (5.7 mg, 0.012 mmol) in THF (0.24 mL) at room temperature was added TBAF (14 μL, 1*M* solution in THF, 0.014 mmol) and the resulting solution was stirred at room temperature for 12 h. The reaction mixture was diluted with Et_2O (0.30 mL) and the organic phase was washed with H_2O (0.30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash chromatography (20% Et_2O in hexanes)

afforded alcohol **240** (3.5 mg, 81%) as a colorless oil: $[\alpha]_D^{20}$ -12.1 (*c* 0.19, $CHCl_3$); IR (neat) 3453 (br), 2977, 2920, 2850, 1640, 1362, 1144, 996, 970, 850; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.30 (s, 12H), 1.86 (s, 3H), 2.38-2.51 (m, 2H), 4.30 (br s, 1H), 5.59 (d, *J* = 10.0 Hz, 1H), 6.36 (s, 1H), 6.57 (dt, *J* = 4.0, 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 20.2, 24.8, 42.0, 75.1, 78.8, 83.3, 148.7, 149.0; HRMS (ES) calcd for $C_{13}H_{23}BIO_3$ $[M+H]^+$ *m/z* 365.0716, found *m/z* 365.0745.

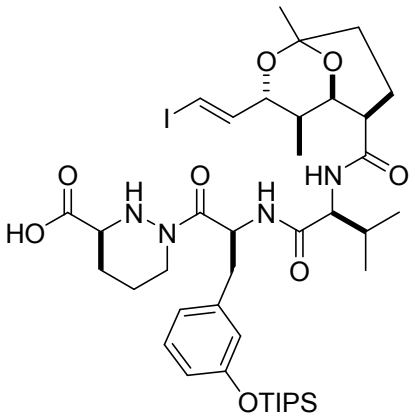


356

(*S*)-Methyl 1-((*S*)-2-((*S*)-2-((3*R*,4*R*,5*R*,6*R*)-3-((*E*)-2-Iodovinyl)-1,4-dimethyl-2,9-dioxa-bicyclo[3.3.1]nonane-6-carboxamido)-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoyl)piperazine-3-carboxylate (356)

To a stirred solution of tripeptide **241** (26.5 mg, 0.0753 mmol), carboxylic acid **242** (50.8 mg, 0.0903 mmol) and HATU (30.0 mg, 0.0790 mmol) in acetonitrile (2.5 mL) at room temperature was added DIPEA (14.4 μL, 0.0828 mmol) and the resulting mixture was stirred for 29 h. The reaction was quenched with pH 7 buffer (2.5 mL) and the aqueous phase was extracted with DCM (3 x 3.0 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*.

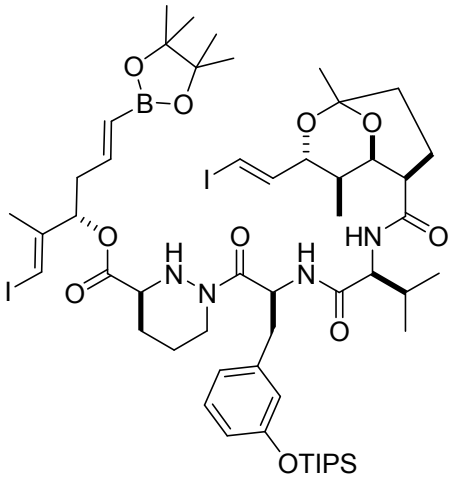
Purification of the residue by flash chromatography (70% EtOAc in hexanes with 1% Et_3N) afforded methyl ester **356** (57.6 mg, 85%) as a yellow oil: $[\alpha]_D^{20}$ -22.5 (*c* 0.40, $CHCl_3$); IR (neat) 3298, 3216, 3063, 2944, 2867, 1745, 1639, 1604, 1584, 1547, 1485, 1443, 1384, 1277, 1235, 1164, 1128, 1004, 882, 844, 781, 734, 687 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.88 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 7.7 Hz, 18H), 1.23-1.29 (m, 5H), 1.44 (s, 3H), 1.45-1.56 (m, 2H), 1.69 (s, 2H), 1.75-1.85 (m, 2H), 1.94-2.01 (m, 2H), 2.05-2.25 (m, 4H), 2.64-2.66 (m, 2H), 2.83-2.96 (m, 2H), 3.73 (s, 3H), 4.26 (d, *J* = 5.6 Hz, 1H), 4.31 (dd, *J* = 4.9, 8.4 Hz, 1H), 4.45 (dd, *J* = 6.3, 11.2 Hz, 1H), 5.70-5.75 (m, 1H), 6.45-6.48 (m, 2H), 6.70 (s, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 7.12 (t, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) 12.7, 12.8, 17.6, 18.0, 19.5, 22.8, 30.8, 31.0, 36.1, 38.7, 39.6, 41.9, 49.7, 52.2, 57.7, 58.1, 71.8, 79.0, 80.4, 95.7, 118.1, 121.4, 122.4, 129.2, 137.9, 145.3, 156.1, 170.1, 171.6, 172.2, 174.5; HRMS (ES) calcd for $C_{41}H_{66}N_4O_8SiI$ $[M+H]^+$ *m/z* 897.3695, found *m/z* 897.3726.



357

(*S*)-1-((*S*)-2-((*S*)-2-((3*R*,4*R*,5*R*,6*R*)-3-((*E*)-2-Iodovinyl)-1,4-dimethyl-2,9-dioxa-bicyclo[3.3.1]nonane-6-carboxamido)-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoyl)piperazine-3-carboxylic Acid (357)

To a stirred solution of methyl ester **356** (3.7 mg, 4.13 μmol) in a mixture of THF (0.22 mL) and H_2O (0.06 mL) at 0 °C was added $LiOH{\cdot}H_2O$ (0.35 mg, 8.25 μmol) and the resulting mixture was stirred at 0 °C for 1 h. The mixture was diluted with EtOAc (3.9 mL) and washed with 1*M* aqueous NaH_2PO_4 (2 x 1.0 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give carboxylic acid **357** (3.6 mg, 99%) as a colorless viscous oil: IR (neat) 3300-2560 (br), 3061, 2926, 2864, 1750, 1632, 1601, 1584, 1485, 1443, 1384, 1273, 1231, 1163, 1122, 1007, 879, 836, 779, 732, 685 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.87 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 7.7 Hz, 18H), 1.23-1.29 (m, 5H), 1.42 (s, 3H), 1.57-1.65 (m, 2H), 1.69-2.09 (m, 6H), 2.12-2.25 (m, 2H), 2.66-2.67 (m, 1H), 2.89-2.99 (m, 3H), 3.69 (s, 1H), 4.26-4.30 (m, 2H), 4.45 (dd, *J* = 6.3, 11.2 Hz, 1H), 5.80 (br s, 1H), 6.47-6.51 (m, 2H), 6.68 (s, 1H), 6.73 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 7.7 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) 12.7, 12.8, 17.6, 18.0, 19.5, 22.8, 30.8, 32.0, 36.1, 38.6, 39.6, 41.9, 50.1, 57.6, 58.1, 71.8, 79.0, 80.4, 95.7, 118.1, 121.4, 122.4, 129.3, 137.8, 145.2, 156.0, 170.7, 172.1, 173.4, 175.0; HRMS (ES) calcd for $C_{40}H_{64}N_4O_8SiI$ $[M+H]^+$ *m/z* 883.3538, found *m/z* 883.3541. The carboxylic acid was used in the next step without purification.



358

(*S*)-((*S*,1*E*,5*E*)-1-Iodo-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-1,5-dien-3-yl) 1-((*S*)-2-((*S*)-2-((3*R*,4*R*,5*R*,6*R*)-3-((*E*)-2-Iodovinyl)-1,4-dimethyl-2,9-dioxa-bicyclo[3.3.1]nonane-6-carboxamido)-3-methylbutanamido)-3-(3-(triisopropylsilyloxy)phenyl)propanoyl)piperazine-3-carboxylate (358)

To a stirred solution of carboxylic acid **357** (16.2 mg, 18.3 μmol), alcohol **240** (13.4 mg, 36.7 μmol), EDCI (7.0 mg, 36.7 μmol) and 4-pyrrolidinopyridine (0.3 mg, 36.7 μmol) in DCM (0.2 mL) at room temperature was added DIPEA (3.2 μL, 18.3 μmol) and the resulting mixture was stirred for 23 h. The reaction was quenched with H_2O (0.2 mL) and the aqueous layer was extracted with DCM (2 x 1.0 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (40% Et_2O in hexanes to 20% MeOH in DCM) to give ester **358** (11.2 mg, 50%) as a colorless oil: ^{1}H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.85-0.92 (m, 9H), 1.11 (d, *J* = 7.0 Hz, 18H), 1.20-1.35 (m, 5H), 1.31 (s, 12H), 1.40-1.45 (m, 2H), 1.56-1.73 (m, 7H), 1.80-2.00 (m, 5H), 2.01-

2.21 (m, 4H), 2.23 (m, 1H), 2.48-2.62 (m, 2H), 2.91-2.99 (m, 1H), 3.60-3.75 (m, 4H), 4.25-4.50 (m, 3H), 5.35-5.60 (m, 3H), 6.35-6.49 (m, 3H), 6.70-6.85 (m, 2H), 7.10-7.13 (m, 1H), 7.36-7.40 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) 12.7, 14.2, 17.4, 18.0, 19.5, 19.9, 20.2, 22.7, 23.0, 24.8, 25.6, 27.2, 29.5, 30.8, 31.3, 32.0, 35.9, 36.1, 38.8, 39.0, 42.0, 50.2, 57.8, 58.3, 70.6, 71.9, 78.8, 80.2, 81.9, 83.3, 95.7, 113.7, 118.1, 121.1, 122.2, 127.0, 129.2, 129.8, 130.0, 130.1, 137.8, 144.2, 145.3, 146.5, 146.9, 156.0, 170.1, 170.3, 172.0, 174.4; HRMS (ES) calcd for $C_{53}H_{84}N_4O_{10}$SiIB $[M+H]^+$ *m/z* 1229.4139, found *m/z* 1229.4077.

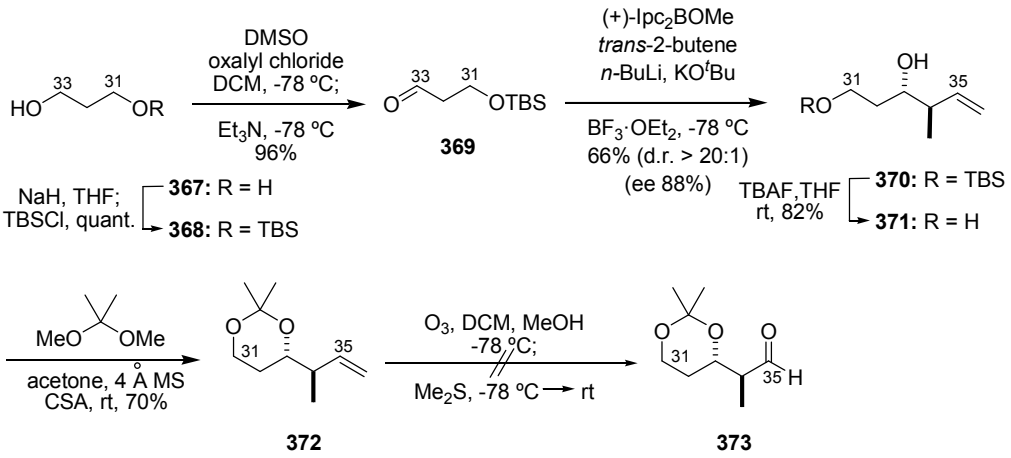
CHAPTER 6: STUDIES TOWARDS THE SYNTHESIS OF THE C26-N42 SPIROLACTAM OF SFA

Synthesis of the spirolactam portion of SFA bearing seven stereogenic centers, six of which are contiguous, presented an especially challenging objective. Our plan for this segment involved initial construction of the C31-C37 substructure as a ω-hydroxy heptaldehyde bearing a correctly configured stereotetrad corresponding to C33, 34, 35 and 36. The remaining carbons, C38-C41, could be added via several routes, only one of which was explored in detail. Final spirolactamization would be accomplished from a suitably constituted 5-oxoundecanamide containing the complete C31-C41 chain. Based on this blueprint, our first target was therefore heptaldehyde **253**.

6.1 Synthesis of the C31-C37 Subunit : Aldehyde 253

Our initial approach to the C31-C37 subunit **253** of SFA began with synthesis of olefin **372**, as illustrated in Scheme 6.1. Exposure of commercially available propane-1,3-diol (**367**) to *tert*-butyldimethylsilyl chloride under basic conditions furnished monosilyl ether **368** which was subjected to Swern oxidation to give aldehyde **369**. Asymmetric crotylation[1] of **369** yielded anti homoallylic alcohol **370**[2] in excellent diastereomeric ratio (> 20:1) and enantiomeric excess (88%). Treatment of **370** with tetra-*n*-butylammonium fluoride afforded diol **371** which was reacted with 2,2-dimethoxypropane in the presence of camphorsulfonic acid to provide acetonide

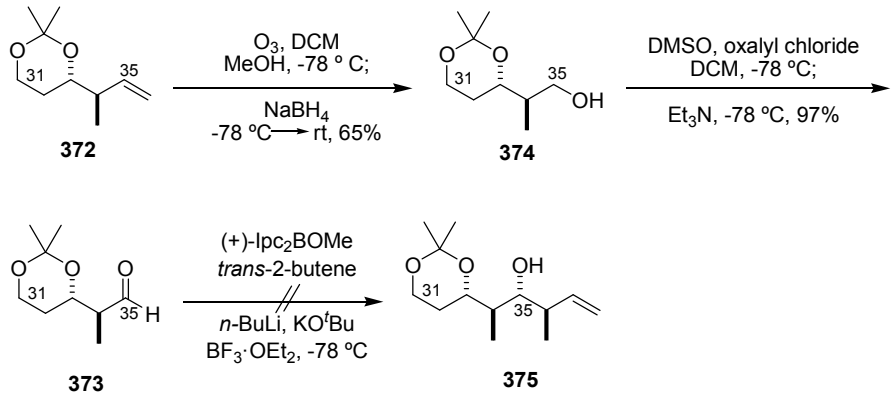
372. However, exposure of **372** to ozone followed by dimethyl sulfide failed to produce aldehyde **373** but instead gave a mixture containing several polar compounds. This unexpected result is presumably due to polymerization of aldehyde **373** after long exposure to dimethyl sulfide during decomposition of the intermediate ozonide.[3]



Scheme 6.1 Synthesis of olefin **372**

In contrast to the attempted ozonolysis of **372** described above, reductive ozonolytic cleavage of this alkene using sodium borohydride as reducing agent gave primary alcohol **374** in good yield. In this manner, reduction of the ozonide generated from **372** directly to alcohol **374** avoided polymerization of aldehyde **373**. Alcohol **374** was oxidized under Swern conditions to aldehyde **373**, as depicted in Scheme 6.2, but subjection of **373** to asymmetric crotylation in the presence of boron trifluoride-ether complex produced an uncharacterizable mixture with no evidence for the formation of homoallylic alcohol **375**. We believe that the acetonide moiety of **373** coordinates with boron trifluoride resulting in cleavage of this protecting group in the

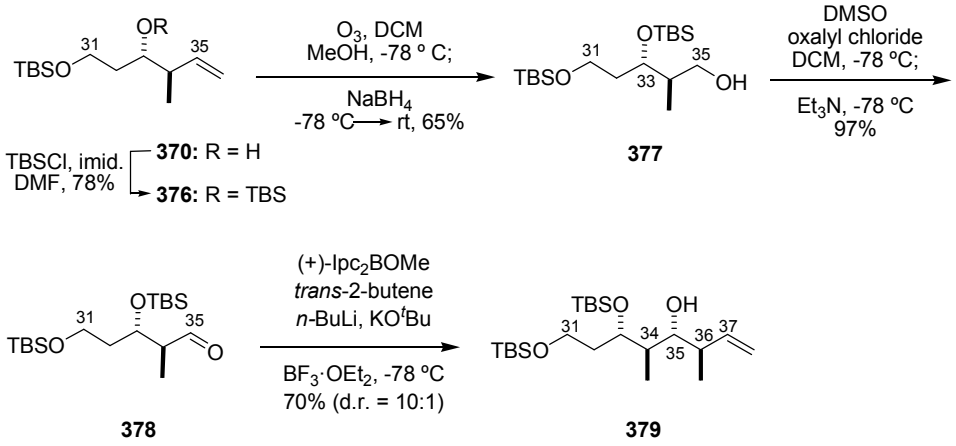
presence of strong nucleophiles such as methoxide anion,[4] and this leads to a complex mixture containing little or no **375**. This conclusion caused us to devise a new route to **253** in which 1,3-diol protection as an acetonide was replaced by individual cover of the C31 and C33 hydroxyl groups as silyl ethers.



Scheme 6.2 Synthesis of aldehyde **373**

Our new route to the C31-C37 portion of SFA is shown in Scheme 6.3 and modifies the previous pathway by replacing the acetonide of **372** with a pair of *tert*-butyldimethylsilyl ethers. Thus, anti homoallylic alcohol **370** was converted to bissilyl ether **376** by treatment with two equivalents of *tert*-butyldimethylsilyl chloride in the presence of imidazole, after which **376** was subjected to reductive ozonolytic cleavage to furnish primary alcohol **377**. The alcohol was oxidized under Swern conditions to aldehyde **378** which upon asymmetric crotylation furnished anti,anti,anti homoallylic alcohol **379** in good yield and with high diastereomeric ratio (10:1) at C35,36. The assignment of configuration to **379** is based upon the previously described crotylation of an aldehyde similar to **378** in Zampella's synthesis of reidispongiolide A.[5] The

transition state that explains attack by the crotylating reagent at the re face of **378** is shown in Figure 6.1.



Scheme 6.3 Synthesis of alcohol **379**

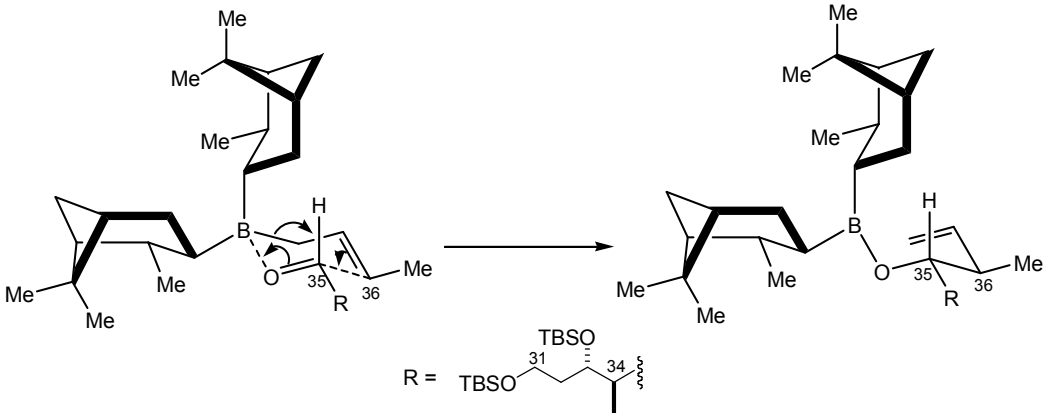
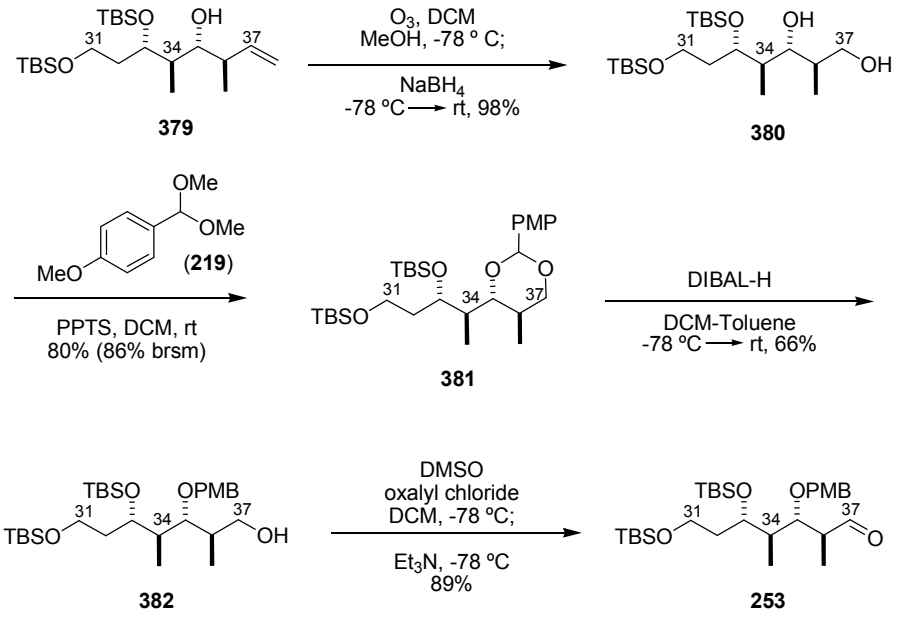


Fig 6.1 Transition state for asymmetric crotylation of aldehyde **378**

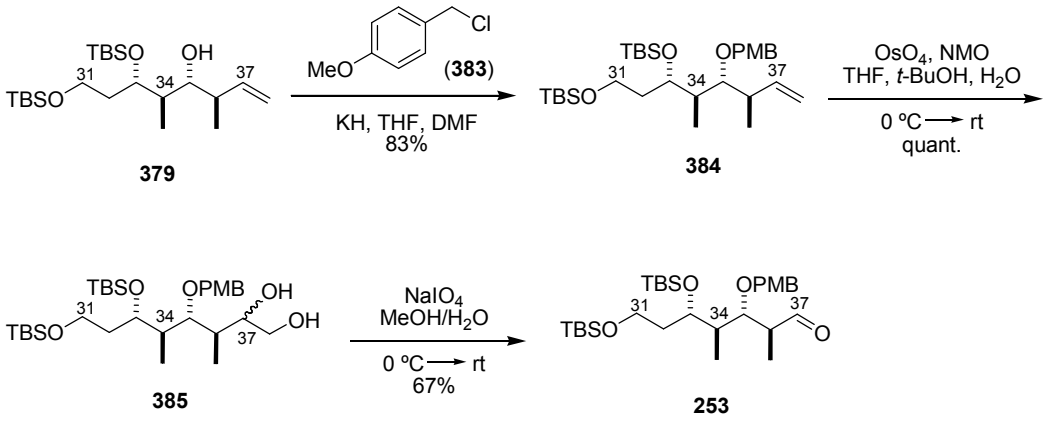
Attempts to protect alcohol **379** as its *p*-methoxybenzyl ether using *p*-methoxybenzyl acetimidate in the presence of triflic acid were unsuccessful. An inseparable mixture of polar compounds was obtained, probably a result of cleavage of one or both *tert*-butyldimethylsilyl ethers under the strongly acidic conditions. A

pathway around this obstacle was found from *p*-methoxybenzyl acetal **381**, a compound obtained from diol **380** by reduction with diisobutylaluminum hydride[6-8] as shown in Scheme 6.4. Thus, reductive ozonolytic cleavage of olefin **379** furnished diol **380** which was reacted with *p*-anisaldehyde dimethyl acetal (**219**) in the presence of pyridinium *p*-toluenesulfonate to give acetal **381**. Treatment of **381** with diisobutylaluminum hydride in a mixture of dichloromethane and toluene resulted in clean reductive scission of the more sterically accessible C-O bond to afford **382**, and Swern oxidation of this primary alcohol delivered aldehyde **253**. Although this route provided usable quantities of **253** for continuing towards our goal of spirolactam **386**, eleven steps were required from propane-1,3-diol (**367**) to reach our target. It was therefore decided to revisit the protection of alcohol **379** in an attempt to bypass acetal **381** and its reduction to **382**, thereby shortening the pathway to **253**.



Scheme 6.4 Synthesis of aldehyde **253** (46% yield, *4 steps*)

After considerable experimentation, it was found that secondary alcohol **379** could be protected as its *p*-methoxybenzyl ether **384** with *p*-methoxybenzyl chloride (**383**) and potassium hydride in a mixture of tetrahydrofuran and *N*,*N*-dimethylformamide (10:1) (Scheme 6.5). The terminal alkene of **384** was oxidized with osmium tetraoxide in the presence of *N*-methylmorpholine-*N*-oxide to produce diol **385** which underwent periodate-mediated glycol cleavage in a mixture of methanol and water to furnish aldehyde **253**. This sequence from **379** was more efficient (56% compared with 46%) and required one less step than that shown in Scheme 6.4.

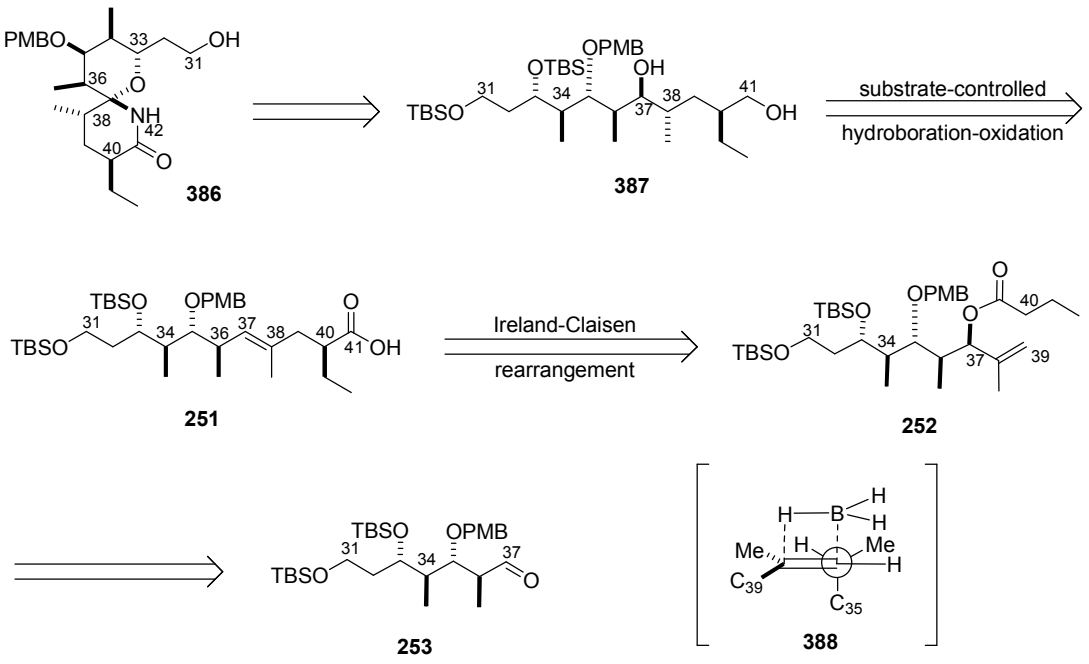


Scheme 6.5 Improved route to aldehyde **253** (56% yield, *3 steps*)

6.2 Towards the Synthesis of C26-N42 Spirolactam 238: An Approach to Spirolactam 386 via Ireland-Claisen Rearrangement

In this approach to spirolactam **386**, our previously prepared aldehyde **253** provides the starting point as shown in the retrosynthetic Scheme 6.6. Spirolactam **386**

would be prepared from diol **387** in which the C37 and C38 stereocenters are set in place via regio- and stereoselective hydroboration-oxidation[9] of carboxylic acid **251**. Transition state **388** leading to addition by borane at the si face of the alkene in **251**, and therefore 37*S* configuration of **387**, should be favored because the preferred conformation of **251** places the largest group on the C36 chiral center perpendicular to the alkene and the attacking borane approaches anti to this group in order to minimize allylic 1,3-strain. An Ireland-Claisen rearrangement[10, 11] of ester **252** would install the C37-C41 carbon framework and introduce the C40 stereocenter of carboxylic acid **251**. Ester **252** would be prepared using a straightforward sequence from aldehyde **253** (Scheme 6.7).

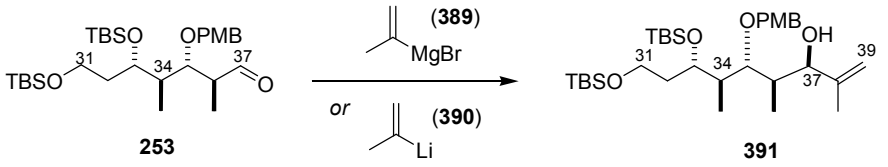


Scheme 6.6 An Ireland-Claisen rearrangement and stereoselective hydroboration strategy for the synthesis of spirolactam **386**

The first step in this plan was introduction of the terminal isopropenyl appendage of **252** by stereoselective addition of an isopropenyl nucleophile to aldehyde **253**.[12, 13] Thus, **253** was treated with commercially available isopropenylmagnesium bromide (**389**) in tetrahydrofuran at 0 °C to give separable allylic alcohols in which the 37*R* diastereomer **391** predominated over the 37*S* stereoisomer by 5:1 (Table 6.1, entry 1). However, an analogous reaction of aldehyde **253** with freshly prepared isopropenyllithium (**390**)[14] in diethyl ether at -78 °C resulted in an enhanced diastereomeric ratio (10:1, Table 6.1, entry 2). This improvement could be due to several factors. First, a lower reaction temperature increases the population of the lowest energy transition state **392** (Figure 6.1) and leads to higher stereoselectivity of addition by the nucleophile. Second, tetrahydrofuran is a stronger Lewis base than diethyl ether and coordinates more strongly with metal ions such as magnesium and lithium; changing the solvent from tetrahydrofuran to diethyl ether therefore reduces solvation of the organometallic reagent and increases coordination of aldehyde **253** to the metal ion. Lastly, lithium ion is more oxyphilic than magnesium and can coordinate more strongly to oxygen atoms in **392**. All three factors would lead to higher stereoselectivity in addition by **390** to **253**. The assignment of *R* configuration at C37 of the major diasteromer was inferred from a Reetz-chelation model[15] and assumes coordination of the organometallic reagent with the *p*-methoxybenzyl ether as shown in Figure 6.2. A half-chair conformation **392** of **253**, which has the C35 alkyl chain in a pseudoequatorial orientation, is the lowest energy transition state and nucleophilic

attack occurs at the si face of the aldehyde. This generates *R* configuration at C37 with **393** emerging in a chair conformation. Attack at the re face of aldehyde **253** would result in a less stable product with a twist-boat conformation.

Table 6.1 Nucleophilic addition to aldehyde **253**



Entry	Conditions	Yield of 391 (%)	d.r.
1	**389**, tetrahydrofuran, 0 °C → rt	81	5:1
2	**390**, diethyl ether, -78 °C	75	10:1

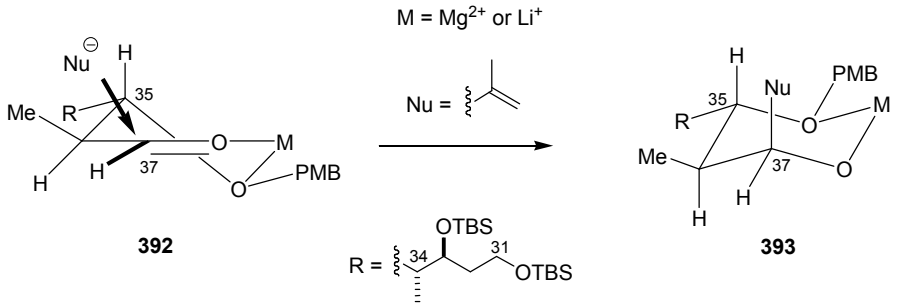
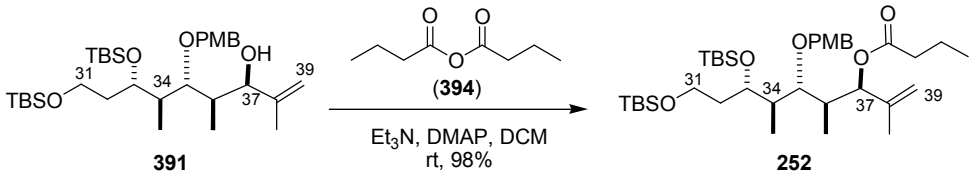


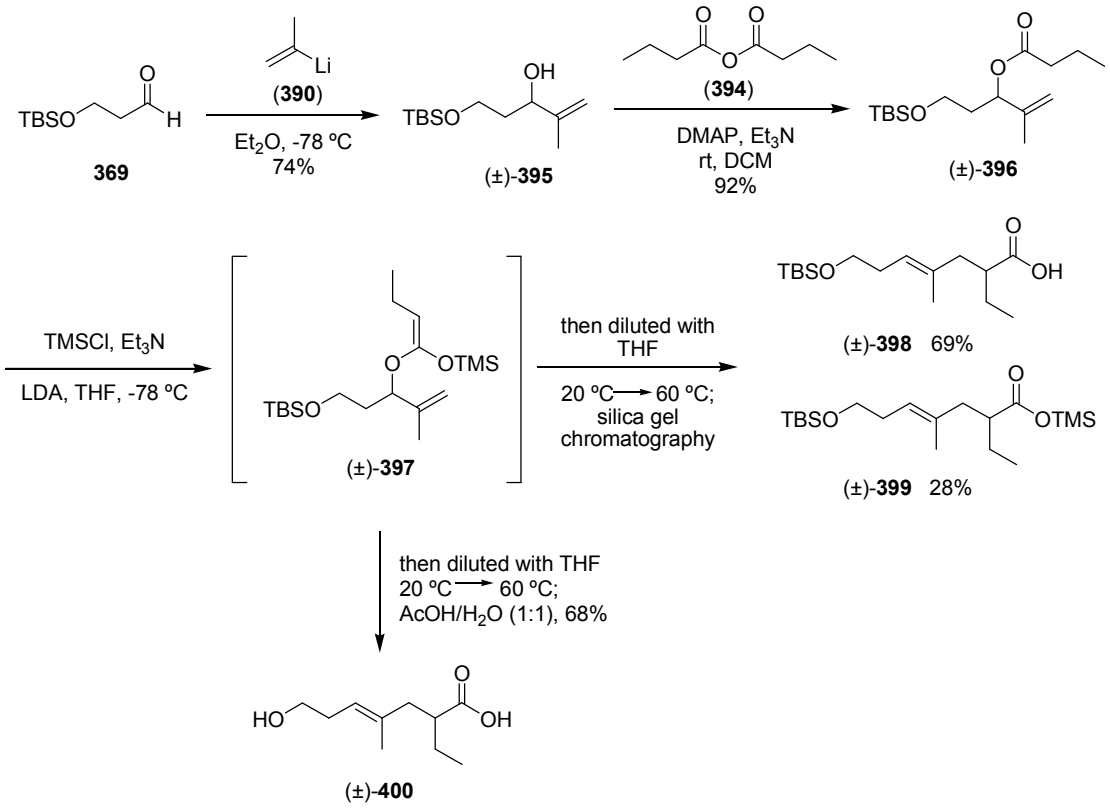
Fig 6.2 Reetz-chelate model for the addition of **390** to **253**

With 37*R* alcohol **391** in hand, ester **389** was prepared by reaction with butyric anhydride (**388**) in the presence of triethylamine and 4-dimethylaminopyridine, as depicted in Scheme 6.7. By contrast, treatment of alcohol **385** with butyryl chloride in the presence of triethylamine led to an uncharacterizable mixture of products.



Scheme 6.7 Synthesis of butyl ester **252**

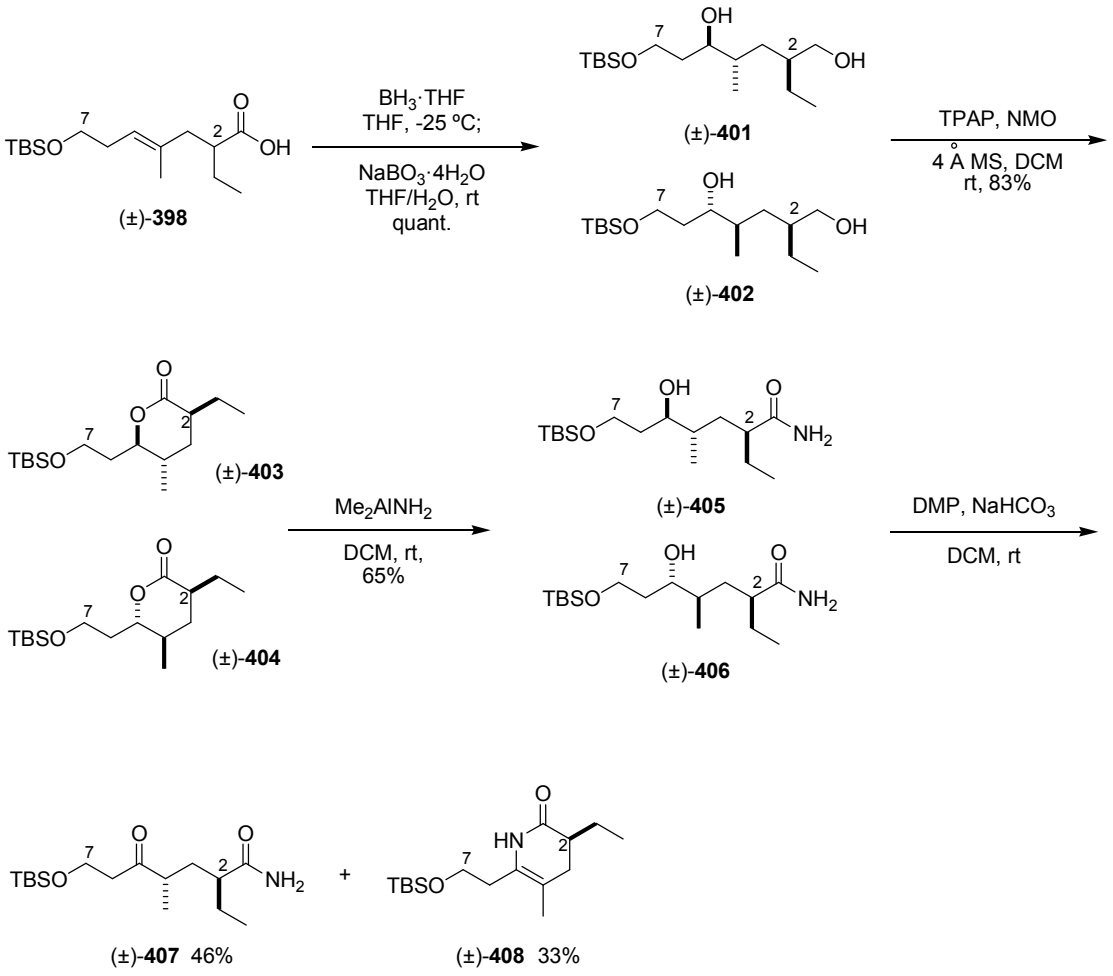
Before investing **252** in a potentially difficult Ireland-Claisen reaction, a model study was conducted on a simpler butyrate ester, as shown in Scheme 6.8. For this experiment, aldehyde **369** was reacted with isopropenyllithium (**390**)[14] to produce allylic alcohol **395** which was esterified with butyric anhydride (**394**) in the presence of 4-dimethylaminopyridine. This afforded ester **396**, the precursor for our model Ireland-Claisen rearrangement.[9, 16] Butyrate ester **396** was reacted with trimethylsilyl chloride, lithium diisopropylamide and triethylamine to give trimethylsilyl ketene acetal **397** as the rearrangement precursor. After diluting the reaction mixture with tetrahydrofuran and heating the solution to reflux, an aqueous ammonium chloride workup of the resulting mixture followed by silica gel chromatography gave rearrangement products in the form of carboxylic acid **398** and trimethylsilyl ester **399**. An alternative acidic work up of the reaction mixture with 1:1:10 acetic acid-water-tetrahydrofuran gave predominantly the hydroxy carboxylic acid **400** in which the *tert*-butyldimethylsilyl ether had been cleaved. Silyl ester **399** was converted to **398** by a second chromatography on silica gel resulting in an overall yield of **398** of 97% from **396**.



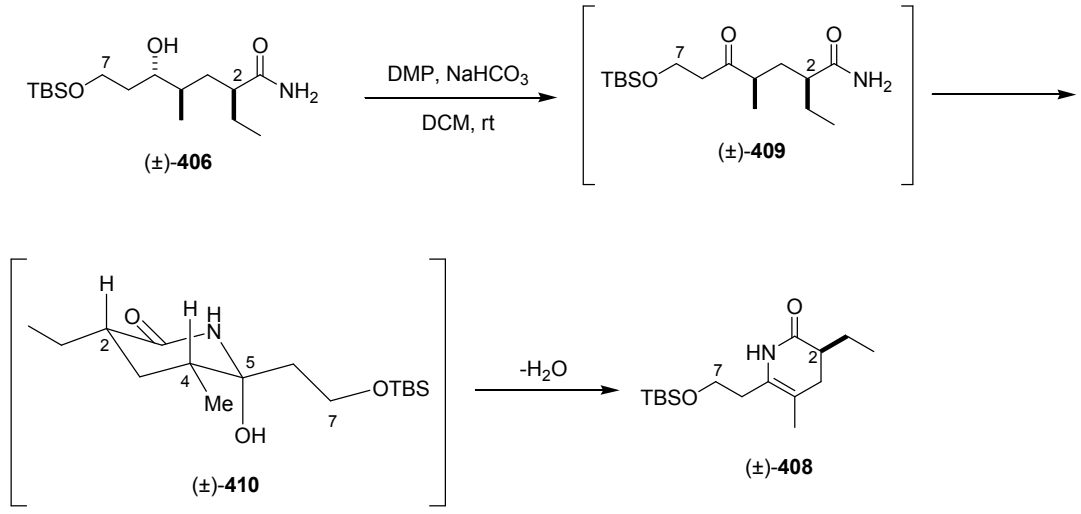
Scheme 6.8 Ireland-Claisen rearrangement of (±)-**396**

The preparation of racemic carboxylic acid **398** enabled us to study the regio- and stereoselectivity of hydroboration-oxidation of its trisubstituted double bond. In the event, subjection of **398** to hydroboration followed by oxidation with sodium perborate gave an inseparable 1:1 mixture of diols **401** and **402** (Scheme 6.9), indicating that the stereogenic center at C2 does not influence hydroboration which therefore occurs at both re and si faces of **398**. Nevertheless, the mixture of **401** and **402** proved useful in guiding strategy as it would apply to **387**, and oxidation of this mixture with tetrapropylammonium perruthenate in the presence of *N*-methylmorpholine-*N*-oxide produced lactones **403** and **404**. Treatment of the lactone

mixture with dimethylaluminum amide[17] yielded hydroxy amides **405** and **406** which upon oxidation with Dess-Martin reagent in the presence of sodium bicarbonate furnished separable keto amide **407** and γ,δ-unsaturated lactam **408**. The formation of lactam **408** results from cyclization of keto amide **409** to hemi-aminal **410** followed by dehydration (Scheme 6.10).

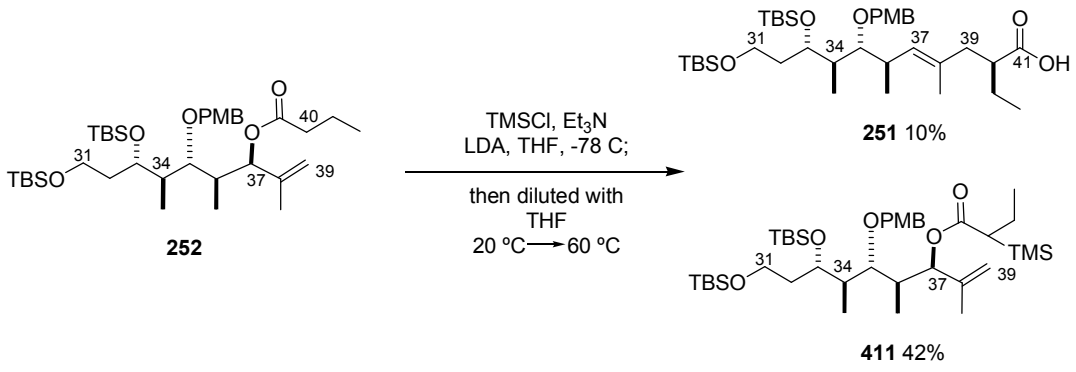


Scheme 6.9 Synthesis of **407** and **408**



Scheme 6.10 Formation of γ,δ-unsaturated lactam **408** from **406**

Our successful Ireland-Claisen rearrangement of **396** to **398** encouraged us to apply the same rearrangement strategy to butyrate ester **252**. However, exposure of **252** to conditions used with **396** resulted in carboxylic acid **251** as only a minor product with α-silyl ester **411** as the predominant product. Formation of 2-trimethylsilyl butyrate **411** from the enolate of **252** with trimethylsilyl chloride and lithium diisopropyl amide is presumably due to steric factors that obstruct *O*-silylation seen with the simpler substrate **396**.[18-20] The 40*S* configuration assigned to **251** results from the chair transition state shown in Figure 6.3 where (*E*)-silyl ketene acetal **412** becomes bonded at its re face.[9] The approach to spirolactam **386** ended at this point due to the low yield of **251** and a paucity of advanced materials.



Scheme 6.11 Synthesis of carboxylic acid **251**

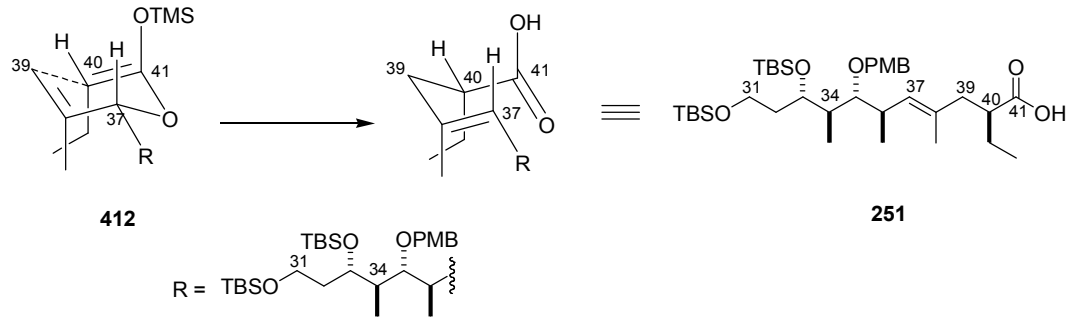


Figure 6.3 An Ireland-Claisen rearrangement of **412** to **251**

Although this approach to the spirolactam portion of SFA ended prematurely, the synthesis of carboxylic acid **251** in low yield gives hope that Ireland-Claisen rearrangement of **252** can offer a viable route to **387** and to spirolactam **386** if the efficiency of the process can be improved. A variety of modifications and improvements have been made to the Ireland-Claisen rearrangement[16,30-31] that would be applicable to **252** and these would be examined with respect to changes in the solvent system and the trialkylsilyl halide. For example, Nicolaou in his approach to the spirolactam portion of SFA (Scheme 2.6) employed *tert*-butyldimethylsilyl

chloride in a tetrahydrofuran-hexamethylphosphoramide solvent pair to prepare silylketene acetal **55** from butyrate **54** and he then transferred **55** to hot toluene in order to complete Ireland-Claisen rearrangement leading to carboxylic acid **56**. These conditions are significantly different from those used with our butyrate **252** and point towards a protocol that ensures efficient formation of a silylketene acetal prior to effecting rearrangement.

The problem revealed in the non-stereoselcetive hydroboration-oxidation of model substrate **398** is not expected to carry over to **251** where stereocenters (at C35 and C36) are positioned to direct addition of borane to the desired *re* face of the C37-C38 alkene. In fact, precedent for good stereoselectivity in the hydroboration-oxidation of **251** can be found in Nicolaou's synthesis of **57** from **58** (Scheme 2.6).[9]

With revisions to our synthesis plan described above, access to spirolactam **386** along lines laid out in Scheme 6.6 seems assured. Alcohol **386** would then stand ready for its assembly into the full Western substructure of SFA.

6.3 References

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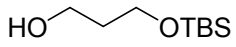
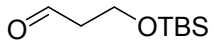
6.4 Experimental Section



368

3-(*tert*-Butyldimethylsilyloxy)propan-1-ol (368)

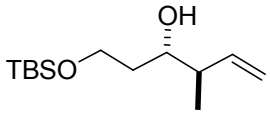
To a stirred suspension of NaH (21.0 g, 0.526 mol, 60% dispersion on mineral oil, washed with hexanes) in THF (1 L) at room temperature was added portionwise neat 1,3-propanediol (40.0 g, 0.526 mol) and the resulting gray suspension was stirred vigorously while H_2 was evolved. After stirring the suspension for 1.5 h, TBSCl (79.2 g, 0.526 mol) was added portionwise and the resulting mixture turned milky as an exothermic reaction occured. The mixture was stirred for 18 h and 10% aqueous Na_2CO_3 (100 mL) was added slowly to quench the reaction. The aqueous phase was extracted with Et_2O (2 x 100 mL) and the combined organic phases were washed with brine (300 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to provide alcohol **368** (101.0 g, quant.) as a colorless oil: IR (neat) 3355, 2955, 2930, 2885, 2858, 1472, 1388, 1361, 1256, 1100, 1006, 962, 939, 872, 837, 815, 776, 721, 662 cm^{-1}; ^1H (400 MHz, $CDCl_3$) δ (ppm) 0.09 (s, 6H), 0.91 (s, 9H), 1.78-1.80 (m, 2H), 2.60 (br s, 1H), 3.81-3.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.5, 18.2, 25.9, 34.2, 62.5, 63.0. The alcohol was used in the next step without purification.



369

3-(*tert*-Butyldimethylsilyloxy)propanal (369)

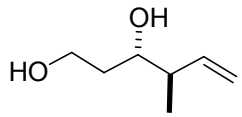
To a stirred solution of oxalyl chloride (0.30 mL, 3.41 mmol) in DCM (24 mL) at -78 °C was added dropwise DMSO (0.41 mL, 5.78 mmol) and the resulting mixture was stirred for 15 min, at which point a solution of alcohol **368** (500 mg, 2.63 mmol) in DCM (4.0 mL) was added slowly. The cloudy mixture was stirred for 10 min and Et_3N (1.83 mL, 13.13 mmol) was added dropwise. The reaction mixture was stirred for 2 h and warmed to 0 °C. H_2O (4.0 mL) was added and the aqueous phase was extracted with DCM (2 x 4.0 mL). The combined organic phase was washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to furnish aldehyde **369** (475 mg, 96%) as a yellow oil: IR (neat) 2956, 2929, 2857, 2715, 1729, 1472, 1389, 1361, 1256, 1099, 970, 836, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.08 (s, 6H), 0.89 (s, 9H), 2.61 (t, J = 6.0 Hz, 2H), 4.00 (t, J = 6.0 Hz, 2H), 9.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.5, 18.2, 25.8, 46.6, 57.4, 202.1. The aldehyde was used in the next step without purification.



370

(3*S*,4*R*)-1-(*tert*-Butyldimethylsilyloxy)-4-methylhex-5-en-3-ol (370)

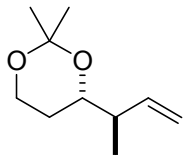
To a stirred suspension of potassium *tert*-butoxide (7.21 g, 64.26 mmol) in dry THF (80 mL) at -78 °C was added *trans*-2-butene (11.1 mL, 123.58 mmol) followed by *n*-butyllithium (1.6*M* in hexanes, 43.3 mL, 69.20 mmol). The resulting yellow solution was stirred at -45 °C for 0.5 h, then cooled to -78 °C and a solution of (+)-B-methoxydiisopinocampheylborane (20.33 g, 64.26 mmol) in THF (80 mL) was added. The mixture was stirred for 1 h, $BF_3 \cdot OEt_2$ (8.54 mL, 69.20 mmol) was introduced slowly, and the solution was stirred for another 0.5 h. A solution of aldehyde **369** (9.31 g, 49.43 mmol) in THF (80 mL) was added, the mixture was stirred for 4 h, and the reaction was quenched at -78 °C with aqueous NaOH (3*N*, 80 mL) followed by 30% aqueous H_2O_2 (80 mL). The mixture was warmed slowly to room temperature and stirred for 3 h. The aqueous layer was separated and extracted with Et_2O (3 x 250 mL) and the combined organic extracts were washed with brine (350 mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash chromatography (15% EtOAc in hexanes) to afford **370** (7.906 g, 66%) as a colorless oil: $[\alpha]_D^{21}$ +10.4 (*c* 1.00, $CHCl_3$); IR (neat) 3446 (br), 2955, 2928, 2857, 1472, 1361, 1255, 1092, 1005, 912, 836, 776 cm^{-1}; ^1H NMR (400 MHz , $CDCl_3$) δ (ppm) 0.09 (s, 9H), 0.92 (s, 9H), 1.06 (d, *J* = 6.8 Hz, 3H), 1.63-1.68 (m, 2H), 2.24-2.29 (m, 1H), 3.24 (br s, 1H), 3.71-3.72 (m, 1H), 3.80-3.85 (m, 1H), 3.90-3.94 (m, 1H), 5.07-5.10 (m, 2H), 5.81-5.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.5, 15.8, 18.2, 25.9, 35.5, 44.0, 62.8, 75.1, 115.1, 140.7; HRMS (CI) calcd for $C_{13}H_{29}O_2Si$ $[M+H]^+$ *m/z* 245.1937, found *m/z* 245.1923.



371

(3*S*,4*R*)-4-Methylhex-5-ene-1,3-diol (371)

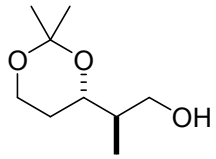
To a stirred solution of TBS ether **370** (6.638 g, 27.18 mmol) in THF (110 mL) at room temperature was added TBAF (32.6 mL, 1*M* solution in THF, 32.6 mmol) and the resulting mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O (50 mL) and the aqueous layer was washed with EtOAc (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (50% EtOAc in hexanes) to give diol **371** (2.892 g, 82%) as a colorless oil: $[\alpha]_D^{20}$ +2.2 (*c* 1.00, $CHCl_3$); IR (neat) 3356, 3075, 2954, 2925, 2867, 2845, 1729, 1640, 1460, 1419, 1375, 1331, 1277, 1127, 1053, 1000, 959, 913, 879, 837, 683 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.03 (d, *J* = 7.2 Hz, 3H), 1.61-1.76 (m, 2H), 2.21-2.26 (m, 1H), 2.79 (br s, 1H), 3.09 (br s, 1H), 3.64-3.67 (m, 1H), 3.78-3.86 (m, 2H), 5.10 (d, *J* = 6.0 Hz, 1H), 5.14 (s, 1H), 5.71-5.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 15.9, 35.3, 44.6, 61.6, 74.9, 116.4, 140.2.



372

(*S*)-4-((*R*)-But-3-en-2-yl)-2,2-dimethyl-1,3-dioxane (372)

To a stirred mixture of diol **371** (1.747 g, 13.42 mmol), camphorsulfonic acid (623.6 mg, 2.68 mmol) and 4 Å MS (2.0 g) in acetone (130 mL) at room temperature was added 2,2-dimethoxypropane (2.5 mL, 20.13 mmol) and the resulting mixture was stirred at room temperature for 16 h. The solvent was evaporated and the residue was diluted with DCM (50 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (30% EtOAc in hexanes) to give acetonide **372** (1.605 g, 70%) as a colorless oil: IR (neat) 2960, 2924, 2854, 1739, 1642, 1462, 1379, 1267, 1241, 1198, 1170, 1101, 1004, 971, 912, 871, 805 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.02 (d, J = 6.8 Hz, 3H), 1.27-1.40 (m, 1H), 1.39 (s, 3H), 1.45 (s, 3H), 1.60-1.72 (m, 1H), 2.21-2.30 (m, 1H), 3.75 (ddd, J = 2.4, 5.2, 11.6 Hz, 1H), 3.85 (ddd, J = 1.6, 5.2, 11.6 Hz, 1H), 3.96 (dt, J = 2.9, 12.0 Hz, 1H), 5.02 (s, 1H), 5.06 (d, J = 5.9 Hz, 1H), 5.82-5.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 14.8, 19.2, 27.9, 29.9, 42.4, 60.0, 72.2, 98.2, 114.4, 140.5.

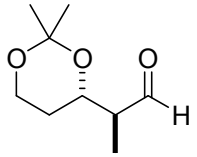


374

(*R*)-2-((*S*)-2,2-Dimethyl-1,3-dioxan-4-yl)propan-1-ol (374)

A solution of acetonide **372** (500 mg, 2.937 mmol) in a mixture of DCM (25 mL) and MeOH (25 mL) was cooled to -78 °C and a steam of ozone was passed through the solution until the starting material was consumed as determined by TLC.

The reaction mixture was purged with argon to remove excess ozone and was treated portionwise at -78 °C with $NaBH_4$ (444 mg, 11.75 mmol). The reaction mixture was warmed slowly to room temperature for 1 h and was concentrated *in vacuo*. The residue was dissolved in EtOAc (50 mL) and the solution was washed with H_2O (30 mL). The aqueous layer was extracted with EtOAc (30 mL) and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (30% EtOAc in hexanes) to provide alcohol **374** (329 mg, 65%) as a colorless oil: IR (neat) 3441 (br), 2991, 2961, 2876, 1460, 1428, 1381, 1271, 1242, 1200, 1171, 1130, 1096, 1033, 994, 970, 899, 873, 850, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.86 (d, J = 7.2 Hz, 3H), 1.39 (s, 3H), 1.45-1.52 (m, 1H), 1.48 (s, 3H), 1.63-1.70 (m, 1H), 1.72-1.80 (m, 1H), 2.96 (br s, 1H), 3.56-3.65 (m, 2H), 3.78-3.89 (m, 2H), 3.98 (dt, J = 2.8, 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 12.8, 19.2, 29.5, 29.9, 40.5, 59.9, 67.6, 75.0, 98.4; HRMS (CI) calcd for $C_9H_{19}O_3$ $[M+H]^+$ *m/z* 175.1334, found *m/z* 175.1334.

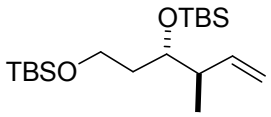


373

(*S*)-2-((*S*)-2,2-Dimethyl-1,3-dioxan-4-yl)propanal (373)

To a stirred solution of oxalyl chloride (0.10 mL, 1.12 mmol) in DCM (1.0 mL) at -78 °C was added dropwise a solution of DMSO (0.10 mL, 1.37 mmol) in DCM (1.0 mL) and the resulting mixture was stirred for 10 min, at which point a solution of alcohol **374** (150 mg, 0.86 mmol) in DCM (1.0 mL) was added dropwise.

After the addition was complete, the solution was stirred for 20 min at -78 °C and Et_3N (0.37 mL, 2.67 mmol) was added slowly. The solution was allowed to warm to -20 °C with stirring over 15 min and H_2O (3.0 mL) was added. The aqueous phase was extracted with DCM (3 x 5.0 mL) and the organic phase was washed with brine (5.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Purification of the residue by flash chromatography (40% Et_2O in hexanes) afforded aldehyde **373** (144 mg, 97%) as a colorless oil: $[\alpha]_D^{20}$ +36.5 (*c* 1.00, $CHCl_3$); IR (neat) 2992, 2933, 2871, 2723, 1728, 1460, 1382, 1272, 1242, 1199, 1171, 1094, 1071, 1044, 968, 878, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.08 (d, *J* = 7.2 Hz, 3H), 1.38 (s, 3H), 1.44-1.53 (m, 1H), 1.48 (s, 3H), 1.68-1.74 (m, 1H), 2.44-2.48 (m, 1H), 3.90 (ddd, *J* = 1.6, 5.6, 12.0 Hz, 1H), 4.01 (dt, *J* = 2.8, 12.0 Hz, 1H), 4.13 (ddd, *J* = 2.4, 7.2, 11.2 Hz, 1H), 9.77 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 9.6, 19.1, 28.7, 29.7, 51.1, 59.7, 70.1, 98.5, 204.3; HRMS (CI) calcd for $C_9H_{16}O_3$ $[M]^+$ *m/z* 172.1100, found *m/z* 175.1106.

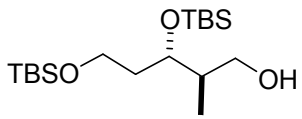


376

(3*R*,4*S*)-4,6-Bis(*tert*-butyldimethylsilyloxy)-3-methylhex-1-ene (376)

To a stirred solution of alcohol **370** (1.00 g, 4.091 mmol) and imidazole (557 mg, 8.182 mmol) in DMF (8.5 mL) at room temperature was added TBSCl (802 mg, 5.318 mmol) and the resulting mixture was stirred at room temperature for 11 h. The reaction was quenched with H_2O (8.5 mL) and extracted with Et_2O (3 x 10 mL). The

combined organic phases were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Flash chromatography of the crude product gave TBS ether **376** (1.150 g, 78%) as a colorless oil: $[\alpha]_D^{20}$ -8.7 (*c* 1.00, $CHCl_3$); IR (neat) 3076, 2960, 2928, 2857, 1640, 1472, 1463, 1387, 1361, 1255, 1100, 1044, 1005, 939, 913, 835, 812, 774, 716, 663 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.06 (s, 3H), 0.07 (s, 3H), 0.07 (s, 6H), 0.91 (s, 9H), 0.91 (s, 9H), 1.02 (d, *J* = 7.2 Hz, 3H), 1.58-1.62 (m, 2H), 2.31-2.35 (m, 1H), 3.60-3.68 (m, 2H), 3.76-3.80 (m, 1H), 5.00 (d, *J* = 4.8 Hz, 1H), 5.03 (s, 1H), 5.75-5.83 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) -5.3, -4.5, 14.7, 18.1, 18.3, 25.9, 26.0, 36.3, 43.3, 60.2, 72.3, 114.4, 140.9; HRMS (CI) calcd for $C_{19}H_{43}O_2Si_2$ $[M+H]^+$ *m/z* 359.2802, found *m/z* 359.2772.

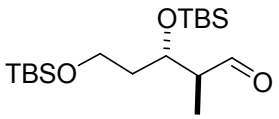


377

(2*R*,3*S*)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-methylpentan-1-ol (377)

A solution of alkene **376** (250 mg, 0.697 mmol) in a mixture of DCM (7.0 mL) and MeOH (7.0 mL) was cooled to -78 °C and a stream of O_3 was bubbled gently through the solution until a light purple color persisted, at which point TLC showed that all of the starting material was consumed. The stream of O_3 was removed and the flask was flushed with argon until the solution was colorless. $NaBH_4$ (106 mg, 2.789 mmol) was added slowly at -78 °C and the mixture was allowed to warm to room temperature. The mixture was concentrated and the residue was dissolved in EtOAc

(14 mL). The organic phase was washed with H_2O (10 mL) and the aqueous layer was extracted with EtOAc (10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated to provide crude product which was purified by flash chromatography (10% EtOAc/hexanes) to give alcohol **377** (163 mg, 65%) as a colorless oil: $[\alpha]_D^{20}$ -3.1 (*c* 1.00, $CHCl_3$); IR (neat) 3388 (br), 2956, 2930, 2885, 2858, 1472, 1463, 1388, 1361, 1256, 1098, 1036, 1006, 939, 836, 812, 775, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.06 (s, 6H), 0.11 (s, 6H), 0.90 (s, 9H), 0.91 (s, 9H), 1.03 (d, *J* = 7.2 Hz, 3H), 1.77-1.82 (m, 3H), 2.67 (br s, 1H), 3.54 (dd, *J* = 5.2, 10.8 Hz, 1H), 3.68 (t, *J* = 6.4 Hz, 2H), 3.79 (dd, *J* = 4.0, 10.8 Hz, 1H), 3.89-3.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.4, -4.7, -4.5, 14.3, 18.0, 18.2, 25.8, 25.9, 37.6, 38.6, 59.7, 65.2, 74.1; HRMS (CI) calcd for $C_{18}H_{43}O_3Si_2$ $[M+H]^+$ *m/z* 363.2751, found *m/z* 363.2752.

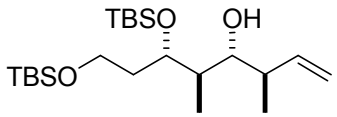


378

(2*S*,3*S*)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-methylpentanal (378)

To a stirred solution of oxalyl chloride (1.56 mL, 17.834 mmol) in DCM (35 mL) at -78 °C was added dropwise a solution of DMSO (2.14 mL, 30.181 mmol) in DCM (25 mL) and the resulting mixture was stirred for 15 min, at which point a solution of alcohol **377** (4.976 g, 13.719 mmol) in DCM (25 mL) was added slowly. The solution was stirred at -78 °C for 20 min and Et_3N (9.57 mL, 68.593 mmol) was added dropwise. The mixture was stirred for 10 min at -78 °C then was allowed to

warm to room temperature. The reaction was quenched with water (60 mL) and the aqueous layer was extracted with DCM (2 x 100 mL). The organic layer was washed with brine (100 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (5% EtOAc/hexanes) to provide aldehyde **378** (4.804 g, 97%) as a colorless oil: $[\alpha]_D^{20}$ +17.3 (*c* 1.00, $CHCl_3$); IR (neat) 2955, 2930, 2885, 2858, 2813, 2710, 1727, 1472, 1463, 1388, 1361, 1256, 1101, 1042, 1006, 939, 837, 812, 776, 712 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.05 (s, 3H), 0.06 (s, 3H), 0.08 (s, 3H), 0.10 (s, 3H), 0.89 (s, 9H), 0.90 (s, 9H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.61-1.83 (m, 2H), 2.54-2.61 (m, 1H), 3.69-3.72 (m, 2H), 4.15-4.19 (m, 1H), 9.75 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.4, -4.8, -4.4, 10.2, 18.0, 18.2, 25.8, 25.9, 37.7, 51.6, 59.1, 70.4, 204.8; HRMS (CI) calcd for $C_{18}H_{40}O_3Si_2$ $[M]^+$ *m/z* 360.2516, found *m/z* 360.2527.

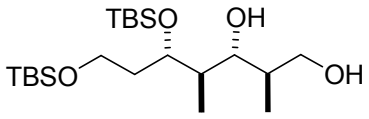


379

(3*R*,4*R*,5*R*,6*S*)-6,8-Bis(*tert*-butyldimethylsilyloxy)-3,5-dimethyloct-1-en-4-ol (379)

To a stirred suspension of potassium *tert*-butoxide (36.4 mg, 0.324 mmol) in dry THF (1.0 mL) at -78 °C was added *trans*-2-butene (60 μL, 0.624 mmol) followed by *n*-butyllithium (1.6*M* in hexanes, 0.22 mL, 0.349 mmol). The resulting yellow solution was stirred at -45 °C for 0.5 h, then cooled to -78 °C and a solution of (+)-B-methoxydiisopinocampheylborane (103 mg, 0.324 mmol) in THF (1.0 mL) was added. The mixture was stirred for 1 h, $BF_3{\cdot}OEt_2$ (43 μL, 0.349 mmol) was introduced

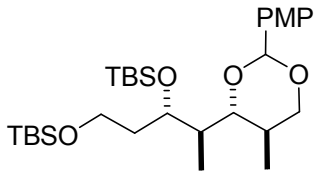
slowly, and the solution was stirred for 0.5 h. A solution of aldehyde **378** (90 g, 0.250 mmol) in THF (1.0 mL) was added, the mixture was stirred for 4 h, and the reaction was quenched at -78 °C with aqueous NaOH (3 *N*, 1.0 mL) followed by 30% aqueous H_2O_2 (1.0 mL). The mixture was warmed slowly to room temperature and stirred for 3 h. The aqueous layer was separated and extracted with Et_2O (3 x 3.0 mL) and the combined organic extracts were washed with brine (5.0 mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash chromatography (20% Et_2O in hexanes) to afford alcohol **379** (73 mg, 70%) as a colorless oil: $[\alpha]_D^{20}$ -4.7 (*c* 1.00, $CHCl_3$); IR (neat) 3501 (br), 3077, 2956, 2885, 2858, 1639, 1472, 1463, 1388, 1361, 1255, 1104, 1048, 1004, 976, 939, 911, 840, 774, 714, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.07 (s, 3H), 0.08 (s, 3H), 0.12 (s, 6H), 0.92 (s, 18H), 0.95 (d, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 7.2 Hz, 3H), 1.75-1.78 (m, 1H), 1.85-1.90 (m, 2H), 2.29-2.38 (m, 1H), 3.49 (s, 1H), 3.60-3.72 (m, 3H), 4.01-4.04 (m, 1H), 5.09-5.16 (m, 2H), 5.88-5.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.3, -4.7, -4.5, -4.4, 10.9, 16.6, 18.0, 18.2, 25.9, 36.3, 37.5, 41.2, 59.7, 74.4, 75.4, 114.4, 142.3; HRMS (ES) calcd for $C_{22}H_{49}O_3Si_2$ $[M+H]^+$ *m/z* 417.3220, found *m/z* 417.3216.



380

(2*R*,3*R*,4*R*,5*S*)-5,7-Bis(*tert*-butyldimethylsilyloxy)-2,4-dimethylheptane-1,3-diol (380)

A solution of alkene **379** (1.847 g, 4.432 mmol) in DCM (22 mL) and MeOH (22 mL) was cooled to -78 °C and a stream of O_3 was bubbled gently through the solution until a light purple color persisted, at which point TLC showed that all of the starting material was consumed. The stream of O_3 was removed and the flask was flushed with argon until the solution was colorless. $NaBH_4$ (503 mg, 13.297 mmol) was then added slowly at -78 °C and the mixture was allowed to warm to room temperature. The mixture was concentrated and EtOAc (40 mL) was added. The organic phase was washed with H_2O (30 mL) and the aqueous phase was extracted with EtOAc (30 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated to provide the crude product which was purified by flash chromatography (10% EtOAc/hexanes) to give diol **380** (1.838 g, 98%) as a colorless oil: IR (neat) 3439 (br), 2956, 2930, 2885, 2858, 1472, 1420, 1387, 1361, 1337, 1255, 1102, 1004, 976, 939, 836, 775, 715, 681, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.06 (s, 3H), 0.07 (s, 3H), 0.14 (s, 6H), 0.75 (d, J = 6.8 Hz, 3H), 0.91 (s, 9H), 0.92 (s, 9H), 1.07 (d, J = 7.2 Hz, 3H), 1.66-1.73 (m, 1H), 1.89-1.93 (m, 3H), 3.56-3.74 (m, 5H), 3.94 (d, J = 9.6 Hz, 1H), 4.03-4.06 (m, 1H), 4.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.5, -5.4, -4.8, -4.4, 11.5, 13.3, 17.9, 18.2, 25.8, 25.9, 35.8, 37.3, 37.9, 59.6, 69.2, 76.6, 77.2; HRMS (ES) calcd for $C_{21}H_{49}O_4Si_2$ $[M+H]^+$ *m/z* 421.3169, found *m/z* 421.3157.

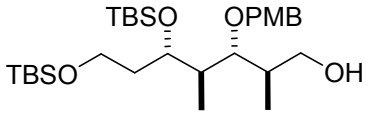


381

(4*R*,5*R*)-4-((2*R*,3*S*)-3,5-Bis(*tert*-butyldimethylsilyloxy)pentan-2-yl)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane (381)

To a stirred solution of diol **380** (479 mg, 1.137 mmol) and PPTS (29 mg, 0.114 mmol) in DCM (4.5 mL) at room temperature was added *p*-anisaldehyde dimethylacetal (0.29 mL, 1.706 mmol) and the reaction mixture was stirred for 5 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (4.5 mL) and the aqueous layer was extracted with DCM (3 x 6.0 mL). The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography (10% EtOAc/hexanes) to afford acetal **381** (394 mg, 80%, 86% brms) as a pale yellow oil: $[\alpha]_D^{20}$ +21.4 (*c* 1.00, $CHCl_3$); IR (neat) 2955, 2929, 2883, 2856, 1616, 1519, 1470, 1463, 1389, 1360, 1302, 1251, 1171, 1121, 1108, 1087, 1039, 1005, 969, 938, 835, 774, 663 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.04 (s, 6H), 0.05 (s, 3H), 0.06 (s, 3H), 0.75 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.93 (s, 9H), 0.97 (d, *J* = 6.8 Hz, 3H), 1.77-1.80 (m, 2H), 1.86-1.90 (m, 1H), 2.03-2.05 (m, 1H), 3.45-3.49 (m, 1H), 3.64-3.78 (m, 3H), 3.82 (s, 3H), 3.88-3.90 (m, 1H), 4.10-4.14 (m, 1H), 5.42 (s, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.3, -5.2, -4.8, -4.1, 8.8, 12.3, 18.1, 18.3, 26.0, 30.3, 36.6,

39.3, 55.3, 59.0, 70.9, 73.4, 82.1, 100.8, 113.5, 127.4, 131.7, 159.7; HRMS (ES) calcd for $C_{29}H_{54}O_5NaSi_2$ $[M+Na]^+$ *m/z* 561.3408, found *m/z* 561.3387.



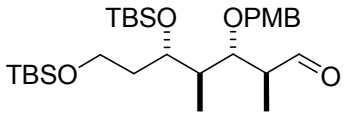
382

(2*R*,3*R*,4*R*,5*S*)-3-(4-Methoxybenzyloxy)-5,7-bis(*tert*-butyldimethylsilyloxy)-2,4-dimethylheptan-1-ol (382)

Method A. To a stirred solution of acetal **381** (440 mg, 0.817 mmol) in DCM (4.0 mL) at -78 °C was added dropwise a solution of DIBAL-H (1*M* solution in hexanes, 2.45 mL, 2.45 mmol) and the resulting mixture was stirred at -78 °C for 45 min, then was allowed to warm to room temperature over 1.5 h. The reaction mixture was quenched with saturated aqueous potassium sodium tartrate (13 mL), the two phases were separated and the aqueous phase was extracted with Et_2O (2 x 20 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (20% EtOAc in hexanes) to provide alcohol **382** (231 mg, 52%) as a pale yellow oil.

Method B. To a stirred solution of acetal **381** (250.4 mg, 0.465 mmol) in DCM (4.6 mL) at –78 °C was added a solution of DIBAL-H (0.30 mL, 1.626 mmol) in toluene (1.6 mL) and the resulting mixture was stirred at –78 °C for 5 min, then was allowed to warm to room temperature over 45 min. The reaction was quenched with MeOH (0.5 mL), and the mixture was diluted with DCM (3.0 mL) and poured into

saturated aqueous potassium sodium tartrate (7.0 mL). The two phases were stirred vigorously and the aqueous phase was extracted with DCM (3 x 10.0 mL). The combined organic layers were washed with brine (15.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Purification of the residue by flash chromatography (20% Et_2O in hexanes) furnished alcohol **382** (159.7 mg, 66%) as a colorless oil: $[\alpha]_D^{20}$ -15.9 (*c* 1.00, $CHCl_3$); IR (neat) 3454, 2955, 2929, 2857, 1614, 1515, 1471, 1388, 1360, 1302, 1251, 1173, 1090, 1039, 1005, 940, 835, 774 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.07 (s, 6H), 0.10 (s, 6H), 0.92 (s, 9H), 0.93 (s, 9H), 2.13 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 7.2 Hz, 3H), 1.62-1.68 (m, 2H), 1.91 (br s, 1H), 1.96-2.01 (m, 1H), 2.82-2.85 (m, 1H), 3.38-3.41 (m, 1H), 3.60-3.74 (m, 3H), 3.83 (s, 3H), 3.83-3.92 (m, 2H), 4.53-4.62 (AB quartet, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.4, -4.4, -4.2, 10.2, 15.7, 18.1, 18.2, 25.8, 25.9, 35.4, 37.3, 42.7, 55.3, 59.5, 65.3, 70.3, 75.4, 86.6, 113.9, 129.4, 130.5, 159.3; HRMS (ES) calcd for $C_{29}H_{57}O_5Si_2$ $[M+H]^+$ *m/z* 541.3745, found *m/z* 541.3749.



253

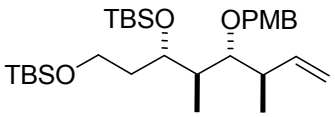
(2*S*,3*S*,4*R*,5*S*)-3-(4-Methoxybenzyloxy)-5,7-bis(*tert*-butyldimethylsilyloxy)-2,4-dimethylheptanal (253)

Method A. To a stirred solution of oxalyl chloride (8.4 μL, 0.096 mmol) in DCM (0.3 mL) at -78 °C was added dropwise a solution of DMSO (11.6 μL, 0.163 mmol) in DCM (0.2 mL) and the resulting mixture was stirred for 10 min, at which

point a solution of alcohol **382** (40 mg, 0.074 mmol) in DCM (0.2 mL) was added slowly. The reaction mixture was stirred at -78 °C for 20 min and Et_3N (52 μL, 0.370 mmol) was added dropwise. The mixture was stirred at -78 °C for 10 min then was warmed to room temperature. The reaction was quenched with water (1.0 mL) and the aqueous layer was extracted with DCM (2 x 2.0 mL). The organic layer was washed with brine (2.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (10% EtOAc in hexanes) to give aldehyde **253** (35.6 mg, 89%) as a colorless oil.

M**ethod B.** To a solution of diol **385** (656.1 mg, 1.149 mmol) in a mixture of THF (10.5 mL) and H_2O (1.0 mL) at room temperature was added $NaIO_4$ (737.4 mg, 3.447 mmol) and the resulting suspension was stirred for 45 min. The mixture was partitioned between Et_2O (10 mL) and H_2O (10 mL) and the aqueous phase was extracted with Et_2O (15 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (5% Et_2O in hexanes) to give aldehyde **253** (413.5 mg, 67%) as a yellow oil: $[\alpha]_D^{20}$ -20.9 (*c* 1.00, $CHCl_3$); IR (neat) 2955, 2930, 2884, 2857, 2720, 1724, 1614, 1587, 1515, 1472, 1388, 1360, 1302, 1251, 1173, 1089, 1039, 1005, 940, 836, 775; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.07 (s, 12H), 0.91 (s, 18H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H), 1.64-1.69 (m, 2H), 1.93-1.96 (m, 1H), 2.71 (br s, 1H), 3.58-3.73 (m, 3H), 3.82 (s, 3H), 3.97 (br s, 1H), 4.50 (A of AB quartet, *J* = 10.4 Hz, 1H), 4.57 (B of AB quartet, *J* = 10.4 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 9.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.4, -4.5, -

4.3, 10.0, 11.9, 18.1, 18.2, 25.9, 35.6, 42.8, 49.5, 55.3, 59.5, 70.2, 74.4, 82.6, 113.8, 129.2, 130.4, 159.2, 204.5; HRMS (ES) calcd for $C_{29}H_{54}O_5NaSi_2$ $[M+Na]^+$ *m/z* 561.3408, found *m/z* 561.3403.

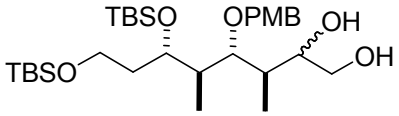


384

1-(((3*R*,4*R*,5*R*,6*S*)-6,8-Bis(*tert*-butyldimethylsilyloxy)-3,5-dimethyloct-1-en-4-yloxy)methyl)-4-methoxybenzene (384)

To a stirred suspension of KH (36.6 mg, 0.912 mmol) in THF (0.50 mL) at 0 °C was added a solution of alcohol **379** (200.0 mg, 0.480 mmol) in THF (0.70 mL) and the mixture was allowed to warm to room temperature with stirring over 1 h. DMF (0.11 mL) and PMBCl (71.6 μL, 0.528 mmol) were added and the resulting mixture was stirred at room temperature for 12 h. The mixture was cooled to 0 °C and the reaction was quenched with saturated aqueous NH_4Cl (1.0 mL). The aqueous phase was extracted with Et_2O (3 x 2.0 mL) and the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (5% EtOAc in hexanes) afforded ether **384** (214.9 mg, 83%) as a colorless oil: $[\alpha]_D^{28}$ -17.2 (*c* 1.00, $CHCl_3$); IR (neat) 3080, 2956, 2929, 2857, 1613, 1514, 1471, 1250, 1172, 1088, 1041, 1005, 940, 835, 774, 665 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.025 (s, 3H), 0.046 (s, 3H), 0.083 (s, 6H), 0.89 (s, 9H), 0.93 (s, 9H), 1.02 (d, *J* = 7.0 Hz, 3H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.51-1.63 (m, 2H), 1.88-1.89 (m, 1H), 2.46-2.52 (m, 1H), 3.13 (dd, *J* = 2.8, 7.7 Hz, 1H), 3.66-3.68 (m, 1H), 3.71-3.73

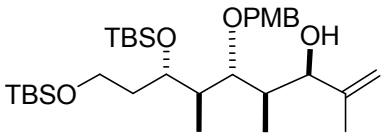
(m, 1H), 3.83 (s, 3H), 3.94-3.95 (m, 1H), 4.52-4.57 (m, 2H), 5.07-5.11 (m, 2H), 5.94-5.98 (m, 1H), 6.90 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) -5.3, -4.7, -4.1, 10.0, 18.1, 18.3, 25.9, 34.6, 41.0, 42.5, 55.3, 60.0, 68.8, 74.9, 85.5, 113.7, 115.1, 129.2, 131.2, 140.5, 159.0; HRMS (CI) calcd for $C_{30}H_{57}O_4NaSi_2$ $[M+H]^+$ *m/z* 537.3795, found *m/z* 537.3783.



385

(3*R*,4*R*,5*R*,6*S*)-4-(4-Methoxybenzyloxy)-6,8-bis(*tert*-butyldimethylsilyloxy)-3,5-dimethyloctane-1,2-diol (385)

To a stirred solution of olefin **384** (200 mg, 0.373 mmol) and NMO (87.3 mg, 0.745 mmol) in a mixture of THF (1.70 mL), *t*-BuOH (1.70 mL) and H_2O (0.34 mL) at 0 °C was added OsO_4 (0.37 mL, 0.05*M* solution in *t*-BuOH, 0.0186 mmol) and the resulting mixture was allowed to warm to room temperature with and was stirred for 22 h. The reaction was quenched with saturated aqueous Na_2SO_3 (3.0 mL) and extracted with EtOAc (3 x 5.0 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the residue by flash chromatography (20% EtOAc in hexanes) afforded diol **385** (217.8 mg, quant.) as a colorless oil: IR (neat) 3428, 2955, 2929, 2857, 1614, 1587, 1515, 1471, 1388, 1361, 1302, 1251, 1173, 1087, 1040, 1006, 940, 836, 775, 665 cm^{-1}; HRMS (CI) calcd for $C_{30}H_{59}O_6Si_2$ $[M+H]^+$ *m/z* 571.3850, found *m/z* 571.3859.



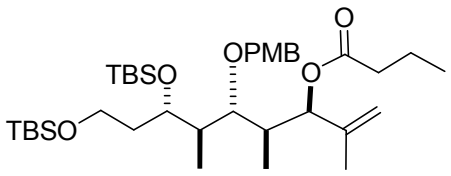
391

(3*R*,4*R*,5*R*,6*R*,7*S*)-5-(4-Methoxybenzyloxy)-7,9-bis(*tert*-butyldimethylsilyloxy)-2,4,6-trimethylnon-1-en-3-ol (391)

M**ethod A.** To a stirred solution of aldehyde **253** (10 mg, 18.6 μmol) in THF (0.5 mL) at 0 °C was added dropwise a solution of isopropenylmagnesium bromide (0.45 μL, 0.5*M* solution in THF, 22.3 μmol) and the resulting solution was stirred at 0 °C for 1.5 h, then was warmed to room temperature over 3 h. The reaction mixture was quenched with H_2O (1.0 mL) and the aqueous phase was extracted with Et_2O (3 x 5.0 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (2.5 mL) and brine, then were dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification of the crude product by flash chromatography (10% EtOAc in hexanes) provided alcohol **391** (8.7 mg, 81%, d.r. 5:1) as a yellow oil.

Method B. Isopropenyllithium (0.5*M* solution in Et_2O, 1.0 mL) was prepared in the following manner. To a stirred solution of *t*-BuLi (1.7*M* in pentane, 0.59 mL, 1.0 mmol) in Et_2O (0.36 mL) at -78 °C was added dropwise 2-bromopropene (44.4 μL, 0.5 mmol) and the resulting mixture was stirred at -78 °C for 35 min, then 0 °C for 5 min.

To a stirred solution of aldehyde **253** (97.0 mg, 0.180 mmol) in Et_2O (0.90 mL) at -78 °C was added isopropenyllithium prepared above (0.5*M* solution in Et_2O, 0.45 mL, 0.225 mmol) and the resulting mixture was stirred at -78 °C for 1.5 h, then was warmed to room temperature over 15 min. The reaction mixture was diluted with Et_2O (1.0 mL) and washed with H_2O (1.0 mL). The aqueous phase was extracted with Et_2O (2 x 1.5 mL) and the combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification of the crude product by flash chromatography (10% EtOAc in hexanes) afforded alcohol **391** (78.8 mg, 75%, d.r. 10:1) as a colorless oil: $[\alpha]_D^{28}$ -19.8 (*c* 1.00, $CHCl_3$); IR (neat) 3489, 2955, 2929, 2884, 2857, 1614, 1515, 1471, 1388, 1360, 1302, 1251, 1174, 1088, 1039, 1005, 940, 900, 835, 775 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.06 (s, 3H), 0.07 (s, 3H), 0.08 (s, 3H), 0.09 (s, 3H), 0.91 (s, 9H), 0.92 (s, 9H), 1.00 (d, *J* = 7.7 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.45-1.51 (m, 1H), 1.58-1.65 (m, 1H), 1.71 (s, 3H), 1.86-1.89 (m, 1H), 2.16-2.19 (m, 1H), 3.40 (dd, *J* = 2.8, 9.1 Hz, 1H), 3.67-3.69 (m, 1H), 3.73-3.75 (m, 1H), 3.83 (s, 3H), 3.84 (s, 1H), 3.92-3.94 (m, 1H), 4.46 (s, 1H), 4.60 (AB quartet, 2H), 4.95 (s, 1H), 5.12 (s, 1H), 6.90 (d, *J* = 9.1 Hz, 2H), 7.30 (d, *J* = 9.1 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) -5.3, -5.2, -4.6, -4.0, 10.6, 11.3, 18.1, 18.4, 20.3, 25.9, 26.0, 34.6, 36.1, 42.4, 55.3, 59.9, 68.9, 73.1, 76.3, 87.6, 110.5, 113.9, 129.4, 130.2, 145.0, 159.3; HRMS (ES) calcd for $C_{32}H_{61}O_5Si_2$ $[M+H]^+$ *m/z* 581.4058, found *m/z* 581.4033.

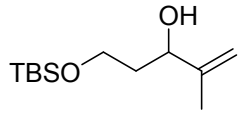


252

(3*R*,4*S*,5*R*,6*R*,7*S*)-5-(4-Methoxybenzyloxy)-7,9-bis(tert-butyldimethylsilyloxy)-2,4,6-trimethylnon-1-en-3-yl Butyrate (252)

To a stirred solution of alcohol **391** (78.0 mg, 0.134 mmol) and DMAP (32.8 mg, 0.269 mmol) in DCM (6.7 mL) at room temperature was added *n*-butyric anhydride (44 μL, 0.269 mmol) followed by Et_3N (94 μL, 0.671 mmol) and the resulting mixture was stirred for 27 h, at which point saturated aqueous $NaHCO_3$ (6.0 mL) was added. The aqueous layer was extracted with DCM (3 x 6.0 mL) and the combined organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification of the crude product by flash chromatography (10% Et_2O in hexanes) gave ester **252** (85.3 mg, 98%) as a colorless oil: $[\alpha]_D^{24}$ -10.7 (*c* 1.00, $CHCl_3$); IR (neat) 2956, 2930, 2857, 1738, 1614, 1515, 1471, 1386, 1360, 1303, 1251, 1180, 1088, 1040, 1005, 940, 836, 774, 665 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.07 (s, 3H), 0.08 (s, 3H), 0.12 (s, 3H), 0.13 (s, 3H), 0.88 (d, *J* = 4.2 Hz, 3H), 0.90 (s, 9H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.93 (s, 9H), 0.99 (t, *J* = 7.0 Hz, 3H), 1.68-1.77 (m, 3H), 1.74 (s, 3H), 1.85-1.91 (m, 2H), 1.92-1.95 (m, 1H), 2.35 (t, *J* = 7.0 Hz, 2H), 3.50 (d, *J* = 8.4 Hz, 1H), 3.70-3.79 (m, 2H), 3.82 (s, 3H), 3.97-4.00 (m, 1H), 4.29 (d, *J* = 9.1 Hz, 1H), 4.51 (d, *J* = 9.1 Hz, 1H), 4.83 (s, 1H), 4.93 (s, 1H), 5.54 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm)

-5.3, -4.2, -3.8, 8.6, 10.4, 13.9, 18.3, 18.5, 20.1, 26.0, 26.1, 36.4, 36.5, 37.4, 41.4, 55.3, 59.2, 72.3, 74.0, 75.6, 80.4, 110.8, 113.7, 129.7, 130.9, 143.0, 159.1, 172.8; HRMS (ES) calcd for $C_{36}H_{67}O_6Si_2$ $[M+H]^+$ *m/z* 651.4476, found *m/z* 651.4455.



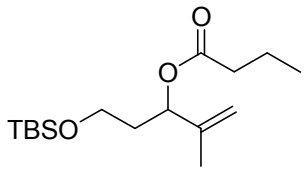
(±)-**395**

5-(*tert*-Butyldimethylsilyloxy)-2-methylpent-1-en-3-ol (395)

Isopropenyllithium (0.5*M* solution in Et_2O) was prepared in the following manner. To a stirred solution of *t*-BuLi (1.8*M* in pentane, 11.1 mL, 20 mmol) in Et_2O (8.0 mL) at -78 °C was added dropwise 2-bromopropene (0.90 mL, 10 mmol) and the resulting mixture was stirred at -78 °C for 35 min.

To a stirred solution of aldehyde **369** (1.497 g, 7.95 mmol) in Et_2O (40.0 mL) at -78 °C was added isopropenyllithium prepared above (0.5*M* solution in Et_2O, 20 mL, 10 mmol) and the resulting mixture was stirred at -78 °C for 1.5 h, then was warmed to room temperature for 15 min. The reaction mixture was diluted with Et_2O (30 mL) and washed with H_2O (50 mL). The aqueous phase was extracted with Et_2O (2 x 50 mL) and the combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification of the crude product by flash chromatography (10% EtOAc in hexanes) afforded alcohol **395** (1.352 g, 74%) as a colorless oil: IR (neat) 3428 (br), 3074, 2954, 2929, 2858, 1651, 1472, 1389, 1361, 1256, 1100, 1006, 939, 899, 835, 812, 776, 732, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.10 (s,

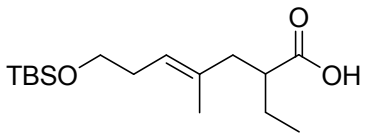
6H), 0.93 (s, 9H), 1.75 (s, 3H), 1.76-1.82 (m, 2H), 3.35 (d, J = 3.2 Hz, 1H), 3.79-3.85 (m, 1H), 3.87-3.92 (m, 1H), 4.27-4.30 (m, 1H), 4.87 (s, 1H), 5.05 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) -5.5, 18.2, 18.5, 25.9, 36.6, 62.3, 75.3, 110.4, 147.0.



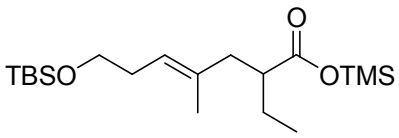
(±)-**396**

5-(*tert*-Butyldimethylsilyloxy)-2-methylpent-1-en-3-yl Butyrate (396)

To a stirred solution of alcohol **395** (281 mg, 1.22 mmol) and DMAP (297 mg, 2.43 mmol) in DCM (2.4 mL) at room temperature was added *n*-butyric anhydride (0.40 mL, 2.43 mmol) followed by Et_3N (0.85 mL, 6.09 mmol) and the resulting mixture was stirred for 12 h, at which point saturated aqueous $NaHCO_3$ (3 mL) was added. The aqueous layer was extracted with DCM (3 x 5 mL) and the organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification of the crude product by flash chromatography (5% EtOAc in hexanes) gave ester **396** (335 mg, 92%) as a colorless oil: IR (neat) 3080, 2958, 2930, 2858, 1741, 1656, 1472, 1362, 1256, 1179, 1101, 954, 903, 836, 776, 665 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.05 (s, 6H), 0.91 (s, 9H), 0.97 (t, J = 7.2 Hz, 3H), 1.65-1.71 (m, 2H), 1.75 (s, 3H), 1.84-1.90 (m, 2H), 2.31 (t, J = 7.6 Hz, 2H), 3.64 (t, J = 6.8 Hz, 2H), 4.89 (s, 1H), 4.97 (s, 1H), 5.29-5.45 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) -5.4, 13.8, 18.2, 18.3, 18.5, 25.9, 36.1, 36.5, 59.3, 74.1, 112.3, 143.5, 172.8.



(±)-**398**



(±)-**399**

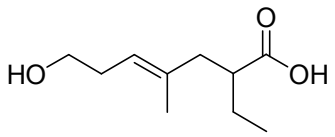
(*E*)-7-(*tert*-Butyldimethylsilyloxy)-2-ethyl-4-methylhept-4-enoic Acid (398) and (*E*)-Trimethylsilyl 7-(*tert*-Butyldimethylsilyloxy)-2-ethyl-4-methylhept-4-enoate (399)

To a stirred solution of ester **396** (1.265 g, 4.21 mmol) in THF (2.8 mL) at -78 °C was added a freshly prepared mixture (1:1 v/v) of trimethylsilyl chloride-triethylamine (5.4 mL), followed by cooled (-30 °C) LDA (5.9 mL, 1.0*M* solution in THF, 5.90 mmol). The reaction mixture was stirred at -78 °C for 2 h, then was warmed to room temperature for 30 min and diluted with THF (10.5 mL). The solution was heated at reflux with stirring for 2 h, then was cooled and diluted with ether (10 mL). The reaction was quenched with saturated aqueous NH_4Cl (15 mL), the aqueous layer was extracted with Et_2O (3 x 20 mL) and the combined organic phases were washed with H_2O (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification of the crude product by flash chromatography (10% EtOAc in hexane) provided carboxylic acid **398** (875 mg, 69%) as a colorless oil along with TMS ester **399** (431 mg, 28%) as a colorless oil.

398: IR (neat) 3300-2500 (br), 2958, 2930, 2858, 1708, 1463, 1255, 1101, 938, 836, 775, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.07 (s, 6H), 0.91 (s, 9H), 0.96 (t, *J* = 7.6 Hz, 3H), 1.53-1.61 (m, 2H), 1.64 (s, 3H), 2.14-2.19 (m, 1H), 2.22-2.27

(m, 2H), 2.33-2.38 (m, 1H), 2.45-2.53 (m, 1H), 3.59 (t, *J* = 7.2 Hz, 2H), 5.21 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.3, 11.7, 15.9, 18.3, 24.7, 25.9, 31.9, 42.0, 45.5, 62.9, 123.2, 133.9, 182.0.

399: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.07 (s, 6H), 0.14 (s, 9H), 0.91 (s, 9H), 1.04 (t, *J* = 7.6 Hz, 3H), 1.50-1.58 (m, 1H), 1.61 (s, 3H), 1.72-1.78 (m, 2H), 2.15 (d, *J* = 14.0 Hz, 1H), 2.24 (m, 2H), 2.85 (d, *J* = 14.0 Hz, 1H), 3.60 (t, *J* = 7.2 Hz, 2H), 5.17-5.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.3, -2.5, 11.3, 16.5, 18.3, 24.3, 26.0, 31.9, 40.9, 43.0, 62.9, 123.9, 135.1, 184.1.

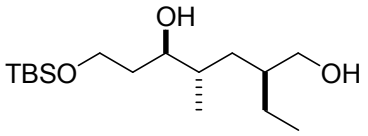


(±)-**400**

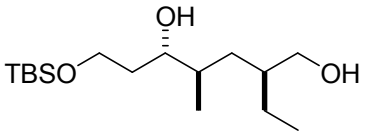
(*E*)-2-Ethyl-7-hydroxy-4-methylhept-4-enoic Acid (400)

To a stirred solution of ester **396** (230 mg, 0.765 mmol) in THF (0.29 mL) at -78 °C was added a freshly prepared mixture (1:1 v/v) of trimethylsilyl chloride-triethylamine (1.16 mL), followed by a cooled (-30 °C) solution of LDA (1.1 mL, 1.0*M* solution in THF, 1.1 mmol). The reaction mixture was stirred at -78 °C for 2 h, then was warmed to room temperature for 30 min and diluted with THF (3.0 mL). The solution was heated at reflux with stirring for 2 h. The reaction was quenched with a mixture (1:1) of AcOH and H_2O (2.5 mL) and the resulting mixture was stirred for 4 h and extracted with Et_2O (3 x 5.0 mL). The organic phase was washed with H_2O (5.0

mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (10% EtOAc in hexane) afforded carboxylic acid **400** (96.6 mg, 68%) as a colorless oil: ^{1}H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.97 (t, *J* = 7.0 Hz, 3H), 1.51-1.55 (m, 1H), 1.65-1.70 (m, 1H), 1.68 (s, 3H), 2.20-2.28 (m, 2H), 2.30-2.36 (m, 2H), 2.50-2.55 (m, 1H), 3.60-3.68 (m, 2H), 5.22 (t, *J* = 7.0 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) 12.0, 16.1, 25.3, 31.2, 42.8, 46.4, 62.2, 122.6, 136.1, 180.8.



(±)-**401**

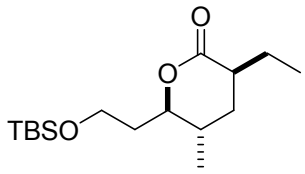


(±)-**402**

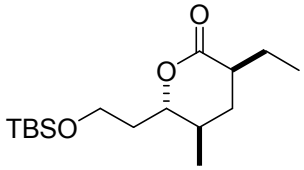
(2*S*,4*S*,5*R*)-7-(*tert*-Butyldimethylsilyloxy)-2-ethyl-4-methylheptane-1,5-diol (401) and (2*S*,4*R*,5*S*)-7-(*tert*-Butyldimethylsilyloxy)-2-ethyl-4-methylheptane-1,5-diol (402)

To a stirred solution of carboxylic acid **398** (100 mg, 0.333 mmol) in THF (0.3 mL) at -25 °C was added BH_3·THF (1.7 mL, 1*M* solution in THF, 1.7 mmol) and the resulting mixture was stirred at that temperature for 2 h. The reaction was quenched with saturated aqueous NH_4Cl (0.17 mL) at -25 °C and a mixture of THF (1.7 mL) and H_2O (1.7 mL) was added followed by $NaBO_3$·$4H_2O$ (1.54 g). The mixture was stirred for 12 h and extracted with EtOAc (3 x 3 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (30% EtOAc in hexane) to give an inseparable ~1:1 mixture of

diols **401** and **402** (112 mg, quant.) as a colorless oil: IR (neat) 3423 (br), 3224 (br), 2929, 2875, 1712, 1463, 1336, 1255, 1094, 836, 776, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.10 (s, 6H), 0.88-0.92 (m, 6H), 0.92 (s, 9H), 1.20-1.71 (m, 8H), 3.55-3.89 (m, 4H), 3.92-3.99 (m, 1H).



(±)-**403**

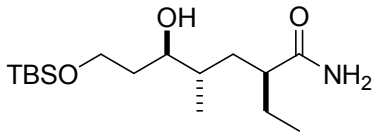


(±)-**404**

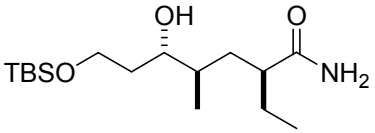
(3*S*,5*S*,6*R*)-6-(2-(*tert*-Butyldimethylsilyloxy)ethyl)-3-ethyl-5-methyl-tetrahydropyran-2-one (403) and (3*S*,5*R*,6*S*)-6-(2-(*tert*-Butyldimethylsilyloxy) ethyl)-3-ethyl-5-methyl-tetrahydropyran-2-one (404)

To a stirred mixture of diols **401** and **402** (14.0 mg, 0.060 mmol), NMO (32.3 mg, 0.276 mmol) and 4 Å MS in DCM (0.92 mL) at room temperature was added TPAP (1.6 mg, 0.0046 mmol) and the resulting mixture was stirred for 1 h. The reaction mixture was filtered through a short silica column and the filtrate was evaporated. The residue was purified by flash chromatography (10% EtOAc in hexane) to afford an inseparable ~1:1 mixture of lactones **403** and **404** (11.5 mg, 83%) as a brown oil: IR (neat) 2958, 2930, 2880, 2858, 1737, 1463, 1385, 1361, 1256, 1190, 1163, 1091, 1006, 939, 836, 812, 777, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.07 and 0.08 (s, 6H), 0.91 (s, 9H), 096-1.05 (m, 6H), 1.41-1.51 (m, 1H), 1.59-1.70 (m, 3H), 1.71-2.01 (m, 3H), 2.35-2.46 (m, 1H), 3.78-3.85 (m, 2H), 4.03-4.11 (m, 1H);

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.3, 11.0 and 11.6, 17.5 and 18.0, 18.3, 23.9 and 24.8, 25.9, 29.7, 31.6, 32.6, 33.5, 34.2, 36.4, 36.8, 39.0, 42.2, 58.7 and 58.8, 79.9 and 83.5, 173.8 and 175.8.



(±)-**405**

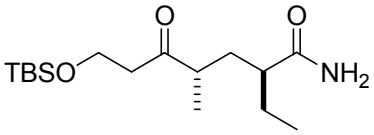


(±)-**406**

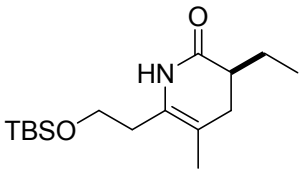
(2*S*,4*S*,5*R*)-7-(*tert*-Butyldimethylsilyloxy)-2-ethyl-5-hydroxy-4-methylheptanamide (405) and (2*S*,4*R*,5*S*)-7-(*tert*-Butyldimethylsilyloxy)-2-ethyl-5-hydroxy-4-methylheptanamide (406)

To a stirred solution of lactones **403** and **404** (46.6 mg, 0.155 mmol) in DCM (6.5 mL) at room temperature was added freshly prepared Me_2AlNH_2 (1.6 mL, 1.2*M* solution in DCM, 1.86 mmol) and the cloudy mixture was stirred for 3.5 h. The mixture was diluted with DCM (3 mL) and the reaction was quenched with saturated aqueous NH_4Cl (6 mL) followed by saturated aqueous sodium potassium tartrate (5 mL). The mixture was stirred for 1 h and the aqueous layer was extracted with DCM (2 x 10 mL). The combined organic phase was washed with brine (15 mL), dried over anhydrous $NaSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by flash chromatography (50% EtOAc in hexanes with 1% Et_3N) furnished an inseparable ~1:1 mixture of amides **405** and **406** (30.5 mg, 65%) as a colorless oil: IR (neat) 3350 (br), 3200, 2957, 2929, 2857, 1666, 1463, 1416, 1387, 1361, 1299, 1255, 1090, 1006, 939, 836, 812, 777, 665 cm^{-1}; ^{1}H NMR (400 MHz,

$CDCl_3$) δ (ppm) 0.09 (s, 6H), 0.82-0.95 (m, 6H), 0.91 (s, 9H), 1.45-1.68 (m, 6H), 1.85-1.96 (m, 1H), 2.19-2.48 (m, 1H), 3.61-3.67 (m, 1H), 3.79-3.82 (m, 1H), 3.89-3.95 (m, 1H), 5.68 (br s, 1H), 5.96 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.5, 11.9, 15.9 and 16.3, 18.1, 25.9, 27.1, 34.9 and 35.0, 36.8 and 37.2, 46.3 and 46.7, 63.3, 76.7 and 77.0, 178.5 and 179.2.



(±)-**407**



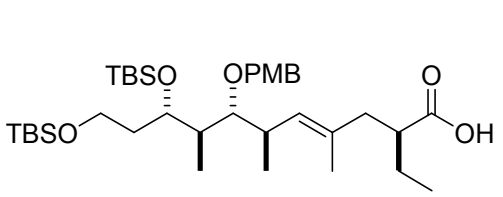
(±)-**408**

(2*S*,4*S*)-7-(*tert*-Butyldimethylsilyloxy)-2-ethyl-4-methyl-5-oxoheptanamide (407) and (*S*)-6-(2-(*tert*-Butyldimethylsilyloxy)ethyl)-3-ethyl-5-methyl-3,4-dihydropyridin-2(1H)-one (408)

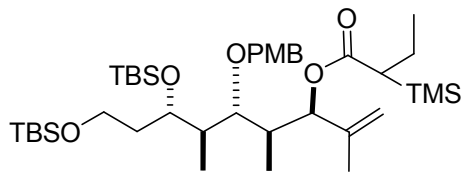
To a stirred mixture of amides **405** and **406** (10.4 mg, 0.0328 mmol) and $NaHCO_3$ (8.3 mg, 0.0983 mmol) in DCM at 0 °C was added Dess-Martin periodinane (20.8 mg, 0.0491 mmol) and the resulting mixture was allowed to warm to room temperature over 2 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (1 mL) and $NaHCO_3$ (1 mL). The aqueous phase was extracted with DCM (3 x 2 mL) and the organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the crude product by flash chromatography (50% EtOAc in hexane) gave amide **407** (4.8 mg, 46%) as a colorless oil and lactam **408** (3.2 mg, 33%) as a colorless oil.

407: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.09 (s, 6H), 0.95-0.99 (m, 3H), 0.92 (s, 9H), 1.11 (d, *J* = 7.2 Hz, 3H), 1.40-1.70 (m, 4H), 1.80-2.10 (m, 2H), 2.20-2.35 (m, 1H), 2.65-2.75 (m, 1H), 3.89-3.96 (m, 1H), 3.97-4.02 (m, 1H), 5.73 (br s, 1H), 5.92 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.3, 12.0, 17.5, 22.7, 29.7, 32.0, 35.2, 43.5, 44.2, 45.9, 58.7, 178.0, 213.5.

408: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.08 (s, 6H), 0.92 (s, 9H), 0.99 (t, *J* = 7.2 Hz, 3H), 1.40-1.51 (m, 2H), 1.72 (s, 3H), 1.72-180 (m, 1H), 2.01-2.11 (m, 1H), 2.23-2.35 (m, 3H), 3.72-3.75 (m, 2H), 7.15 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) -5.5, 11.5, 17.3, 18.2, 22.7, 25.9, 32.3, 32.4, 41.1, 62.1, 108.1, 128.1, 173.1.



251



411

(2*S*,6*R*,7*R*,8*R*,9*S*,*E*)-7-(4-Methoxybenzyloxy)-9,11-bis(*tert*-butyldimethylsilyloxy)-2-ethyl-4,6,8-trimethylundec-4-enoic Acid (251) and (3*R*,4*S*,5*R*,6*R*,7*S*)-5-(4-Methoxybenzyloxy)-7,9-bis(*tert*-butyldimethylsilyloxy)-2,4,6-trimethylnon-1-en-3-yl 2-(Trimethylsilyl)butanoate (411)

To a stirred solution of ester **252** (84.0 mg, 0.129 mmol) in THF (0.05 mL) at -78 °C was added a freshly prepared mixture (1:1 v/v) of trimethylsilyl chloride-triethylamine (0.20 mL), followed by a cooled (-30 °C) solution of LDA (0.18 mL, 1.0*M* solution in THF, 0.18 mmol). The reaction mixture was stirred at -78 °C for 2 h,

then was warmed to room temperature for 30 min and diluted with THF (1.0 mL). The solution was heated at reflux with stirring for 4 h, then was cooled and diluted with Et_2O (2.0 mL). A mixture of H_2O (0.25 mL) and AcOH (0.25 mL) was added and the resulting mixture was stirred overnight and extracted with Et_2O (3 x 3.0 mL). The combined organic phase was washed with H_2O (2.0 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. Purification of the crude product by flash chromatography (5% EtoAc in hexane) provided carboxylic acid **251** (8.3 mg, 10%) as a colorless oil and ester **411** (35.4 mg, 42%) as a colorless oil.

251: $[\alpha]_D^{27}$ -11.6 (*c* 0.95, $CHCl_3$); IR (neat) 3200-2500 (br), 2956, 2929, 2857, 1708, 1612, 1514, 1463, 1387, 1361, 1252, 1171, 1090, 1005, 940, 836, 775 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ (ppm) -0.02 (s, 3H), 0.02 (s, 3H), 0.08 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 0.89-0.91 (m, 6H), 0.94 (s, 9H), 1.00 (d, *J* = 7.0 Hz, 3H), 1.49-1.55 (m, 2H), 1.55-1.63 (m, 2H), 1.65 (s, 3H), 1.78-1.81 (m, 1H), 2.10-2.15 (m, 1H), 2.30-2.33 (m, 1H), 2.5 (br s, 1H), 2.57-2.63 (m, 1H), 3.09-3.12 (m, 1H), 3.60-3.70 (m, 1H), 3.70-3.78 (m, 2H), 3.82 (s, 3H), 4.52 (AB quartet, 2H), 5.40 (d, *J* = 7.7 Hz, 1H), 6.90 (d, *J* = 7.0 Hz, 2H), 7.30 (d, *J* = 7.0 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) -5.2, -4.9, -4.4, 10.1, 12.0, 16.0, 18.1, 18.5, 25.4, 25.9, 34.8, 35.7, 42.8, 42.9, 43.0, 55.3, 60.4, 69.5, 74.8, 85.2, 113.6, 129.1, 129.3, 131.3, 131.9, 159.0, 181.0; HRMS (ES) calcd for $C_{32}H_{67}O_6Si_2$ $[M+H]^+$ *m/z* 651.4476, found *m/z* 651.4483.

411: IR (neat) 2956, 2921, 2857, 1716, 1656, 1614, 1587, 1515, 1471, 1387, 1360, 1344, 1303, 1251, 1223, 1173, 1089, 1038, 1006, 967, 945, 836, 775, 663 cm^{-1};

^{1}H NMR (700 MHz, $CDCl_3$) δ (ppm) 0.06 (s, 3H), 0.07 (s, 3H), 0.11 (s, 3H), 0.12 (s, 3H), 0.14 (s, 9H), 0.88 (d, *J* = 4.2 Hz, 3H), 0.91 (s, 9H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.93 (s, 9H), 0.99 (t, *J* = 7.0 Hz, 3H), 1.50-1.56 (m, 1H), 1.62-1.69 (m, 2H), 1.78 (s, 3H), 1.85-1.91 (m, 3H), 1.98-2.02 (m, 1H), 3.36 (d, *J* = 7.7 Hz, 1H), 3.70-3.79 (m, 2H), 3.82 (s, 3H), 3.97-4.00 (m, 1H), 4.39 (d, *J* = 9.8 Hz, 1H), 4.48 (d, *J* = 9.8 Hz, 1H), 4.95 (s, 1H), 4.97 (s, 1H), 5.57 (d, *J* = 4.9 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ (ppm) -5.4, -4.2, -4.0, -2.1, 7.9, 10.7, 15.4, 18.2, 19.8, 20.4, 26.0, 26.1, 36.0, 37.7, 39.9, 41.1, 55.3, 59.5, 72.5, 73.0, 76.4, 80.4, 112.8, 113.7, 129.6, 130.9, 143.1, 159.0, 174.7; HRMS (ES) calcd for $C_{39}H_{75}O_6Si_3$ $[M+H]^+$ *m/z* 723.4872, found *m/z* 723.4843.

CHAPTER 7: CONCLUSION

The studies described in this dissertation outline a conceptually novel approach to sanglifehrin A. The key features in our approach are a Masamune anti-aldol reaction to set in place the C14-C15 configuration of iodo acid **242**, an asymmetric catalytic phase-transfer method to introduce an α-amino function in the synthesis of L-*m*-tyrosine derivative **331** and a double asymmetric crotylation to assemble an array of alternating oxygen and methyl functionalities along the C33-C36 backbone. Although an attempt to close vinyl boronate **358** to macrolactone **239** using Suzuki-Miyaura cross coupling was unsuccessful, modification of the reaction conditions hold promise for the completion of this subunit of sanglifehrin A. A model study with **396** in which Ireland-Claisen rearrangement was shown to yield **398** could not be extrapolated to butyrate **252** efficiently. This leaves in question our planned route to spirolactam **386** and an eventual total synthesis of SFA along lines laid out in Scheme 3.1. Further studies will be needed before a plausible synthesis of this complex structure can be charted.

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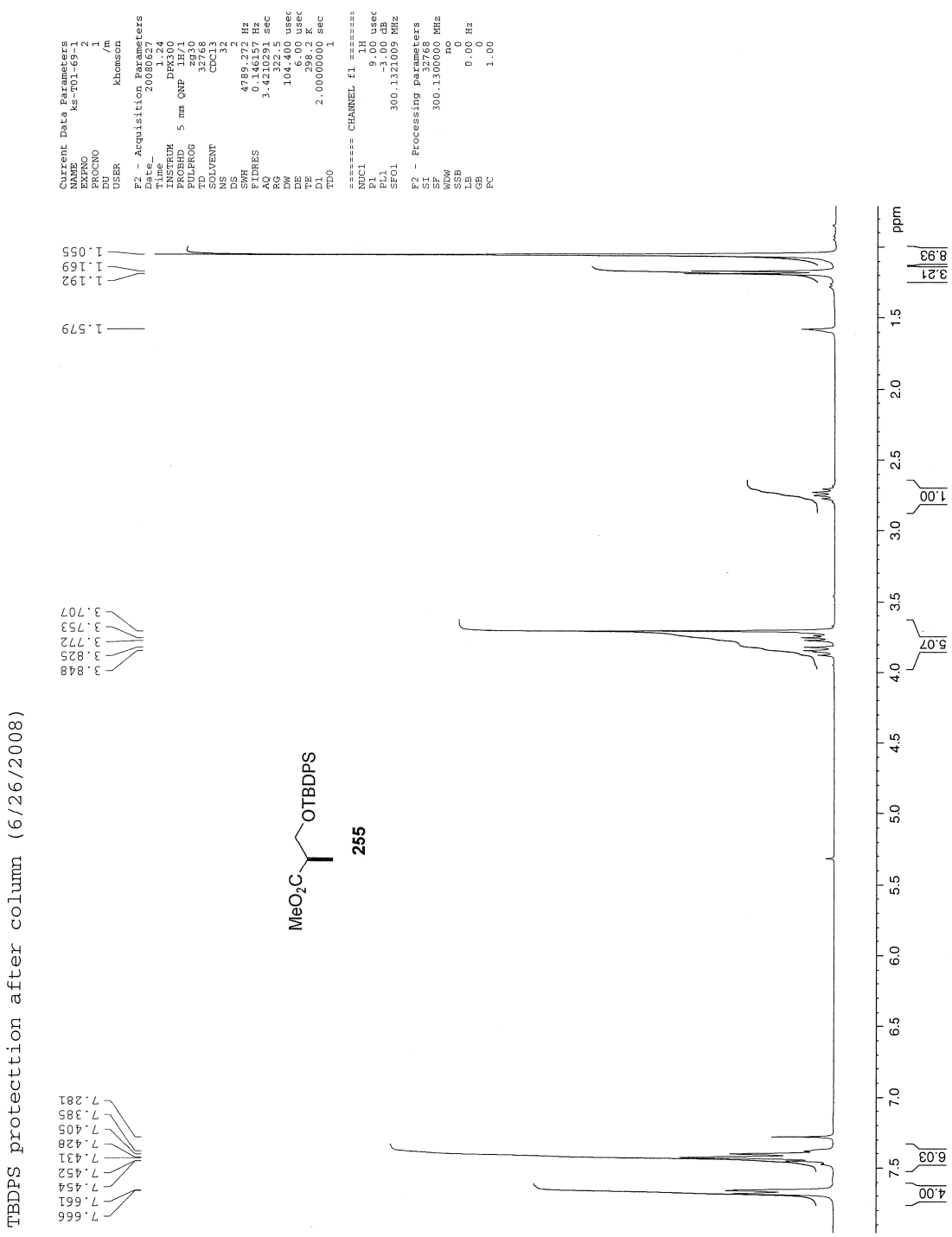
APPENDICES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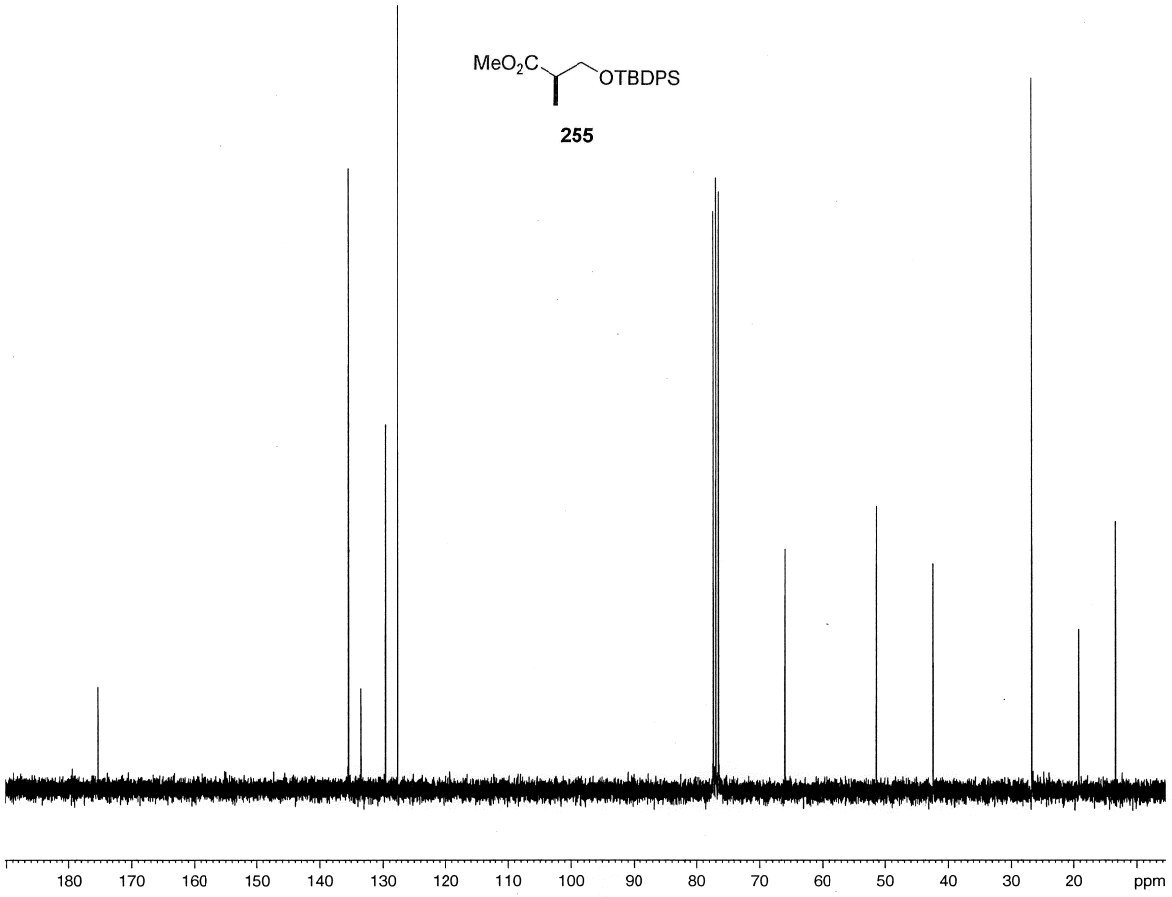


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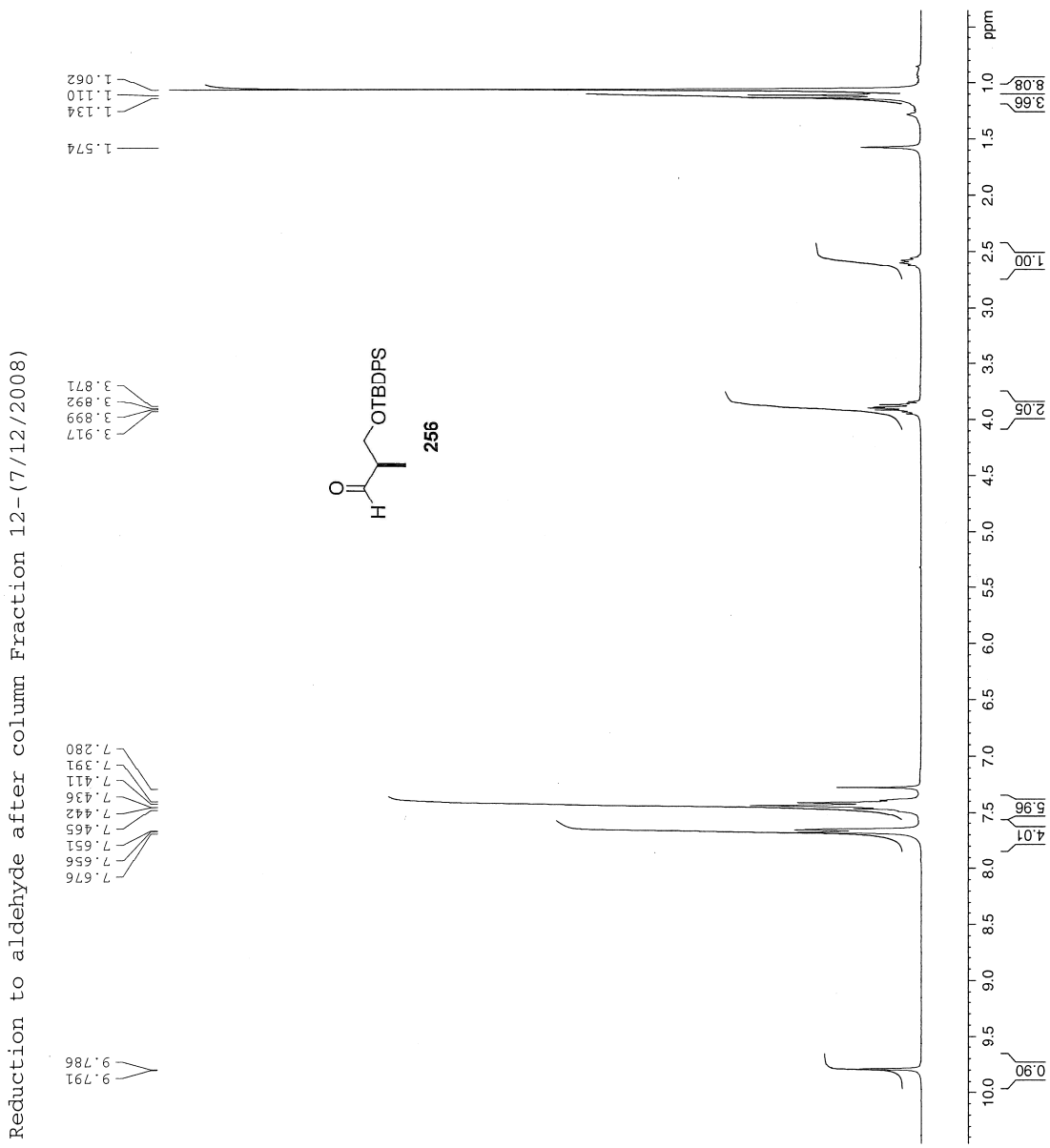
NAME         ks-T01-69-2
EXPNO                  1
PROCNO                 1
DU                    /m
USER             khomson

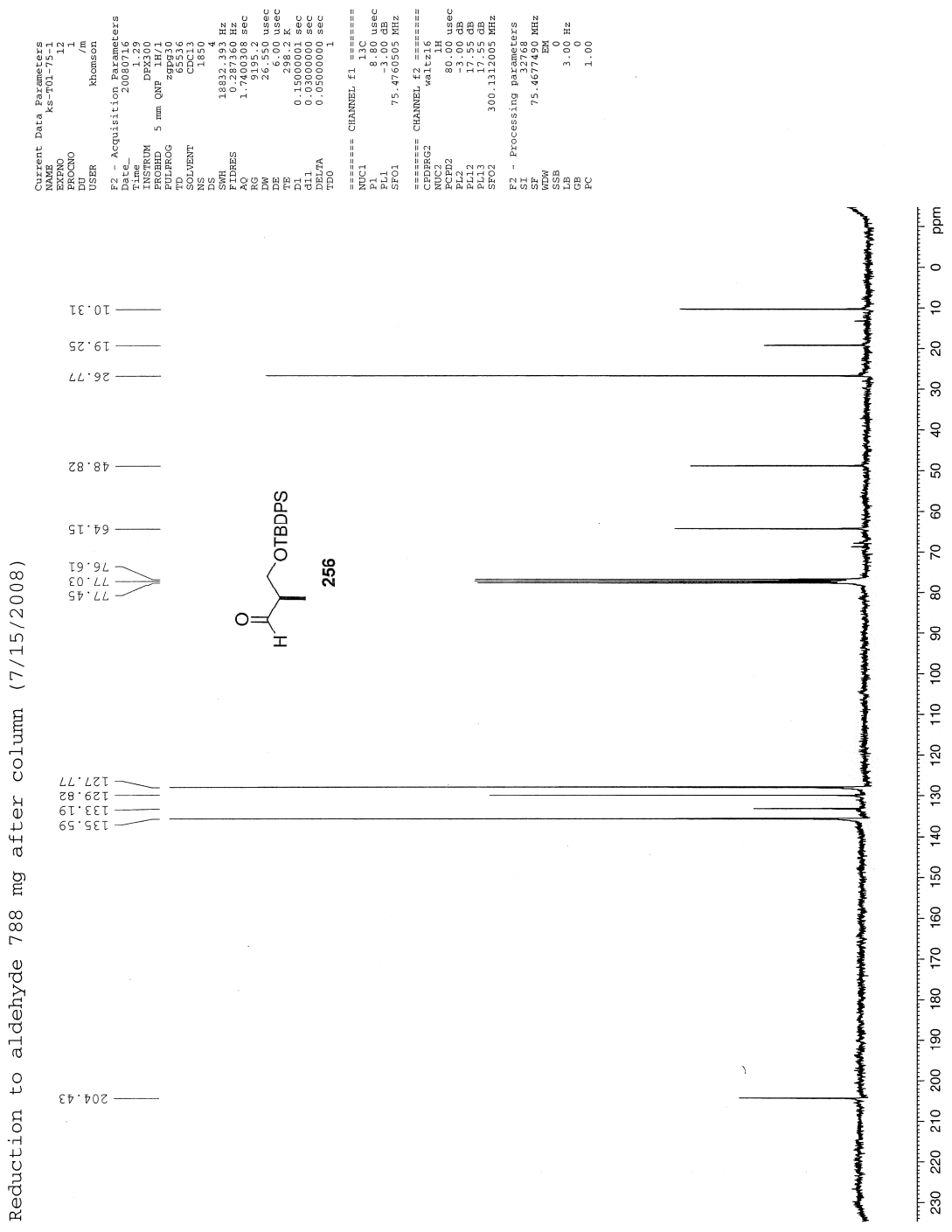
F2 - Acquisition Parameters
Date_             20080627
Time                  2.26
INSTRUM            DPX300
PROBHD   5 mm QNP  1H/1
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1850
DS                     4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 sec
RG                9195.2
DW                26.550 usec
DE                 6.00 usec
TE                298.2 K
D1            0.15000001 sec
d11           0.03000000 sec
DELTA         0.05000000 sec
TD0                    1

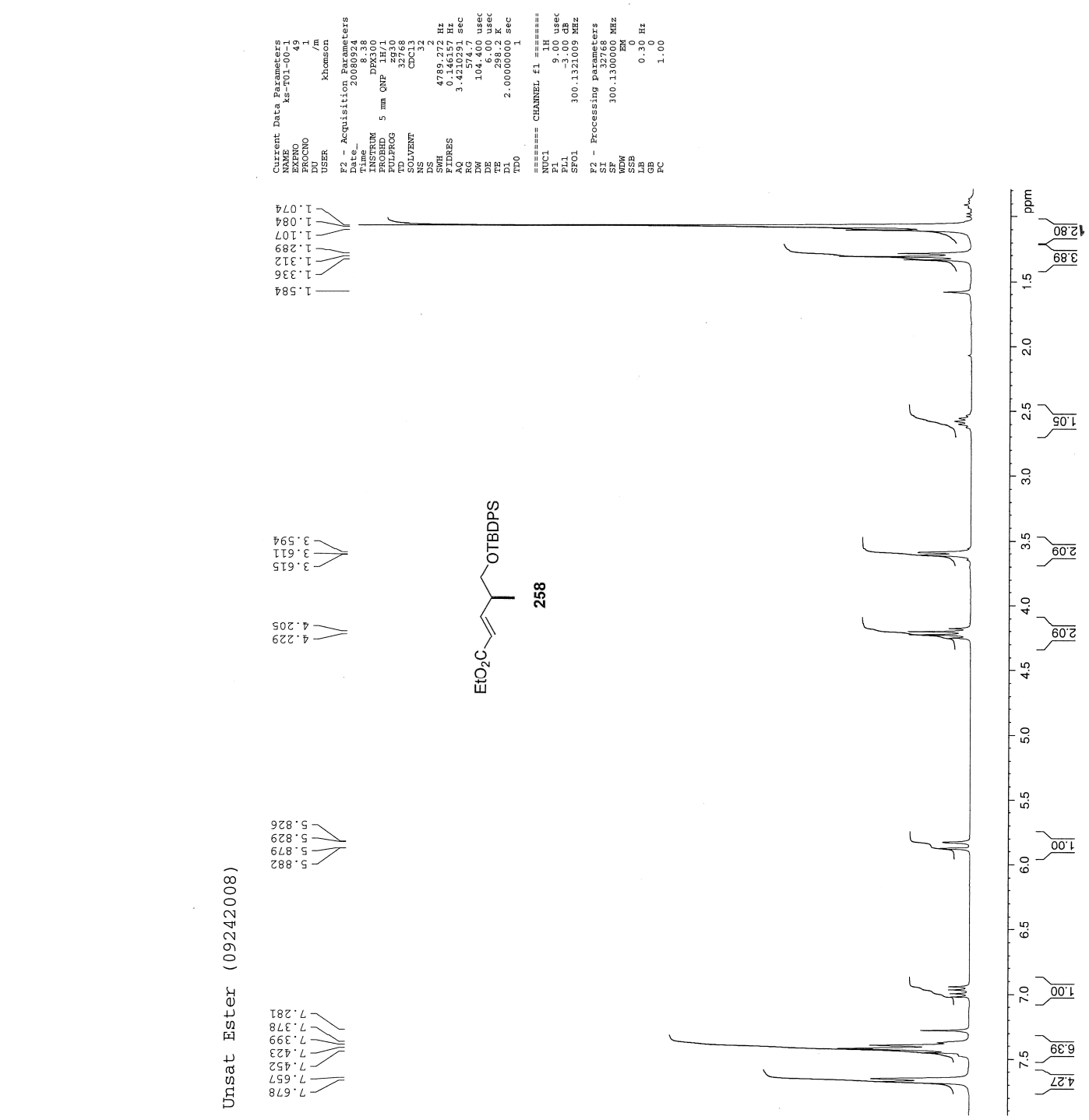
======== CHANNEL f1 ========
NUC1                  13C
P1                   8.80 usec
PL1                 -3.00 dB
SFO1          75.4760505 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2                80.00 usec
PL2                 -3.00 dB
PL12                17.55 dB
PL13                17.55 dB
SFO2          300.1312005 MHz

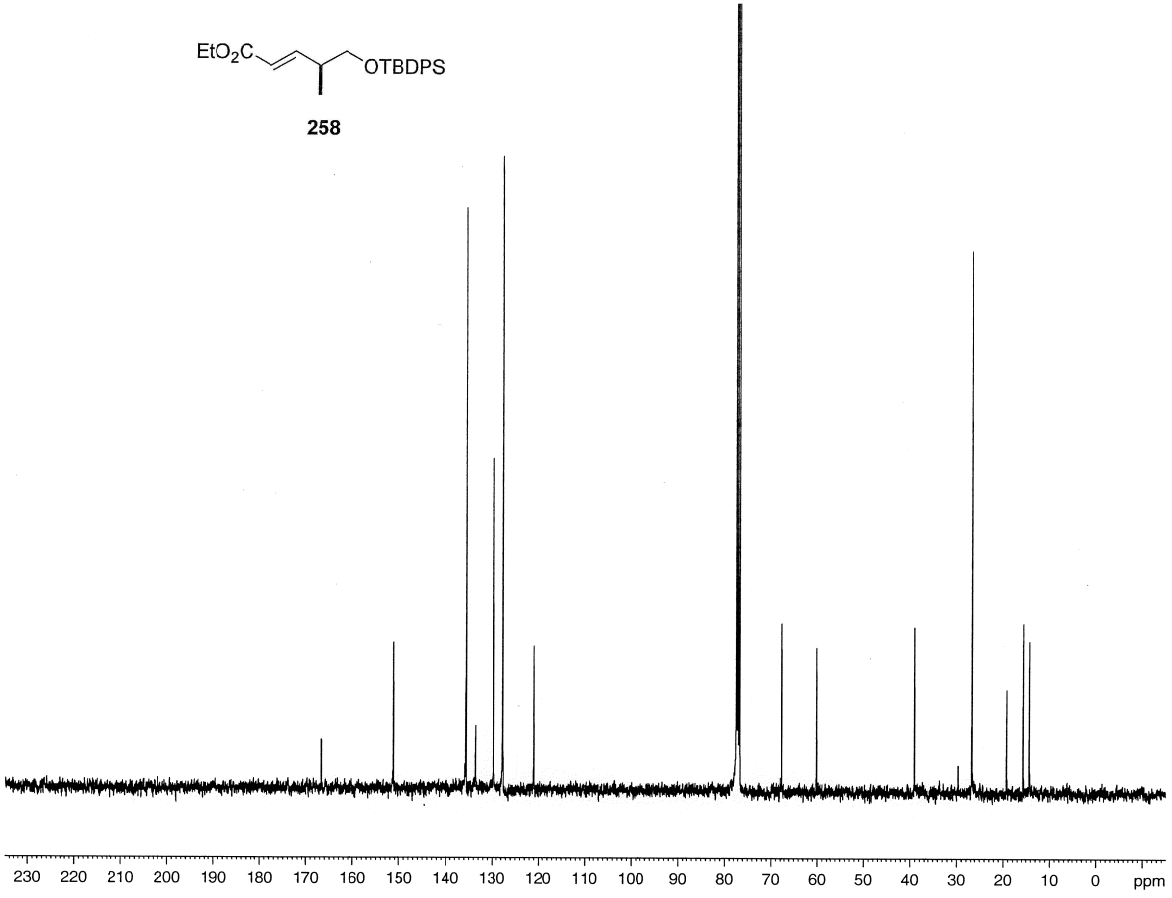
F2 - Processing parameters
SI                 32768
SF            75.4677490 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.40
```


Reduction to aldehyde after column Fraction 12-(7/12/2008)
Current Data Parameters
NAME ks-701-75-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20080712
Time 19.09
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OTBDPS
O
H
256
ppm


Reduction to aldehyde 788 mg after column (7/15/2008)
Current Data Parameters
NAME ks-f01-75-1
EXPNO 12
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20080716
Time 1.29
INSTRUM DFX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1850
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7401038 sec
RG 285.2
DW 26.550 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -3.00 dB
SFO1 75.4760505 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 17.55 dB
PL13 17.55 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 37768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
OTBDPS
256
204.43
135.59
133.19
129.82
127.77
77.45
77.03
76.61
64.15
48.82
26.77
19.25
10.31
ppm


Unsat Ester (09242008)
Current Data Parameters
NAME ks-701-007-1
EXPNO 49
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20080924
Time 8.38
INSTRM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.678
7.657
7.452
7.423
7.399
7.378
7.281
5.882
5.879
5.829
5.826
4.229
4.205
3.615
3.611
3.594
1.584
1.336
1.312
1.289
1.107
1.084
1.074
EtO2C
OTBDPS
258
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
4.27
6.39
1.00
1.00
2.09
2.09
1.05
3.89
12.80

Wittig after column (7/13/2008)



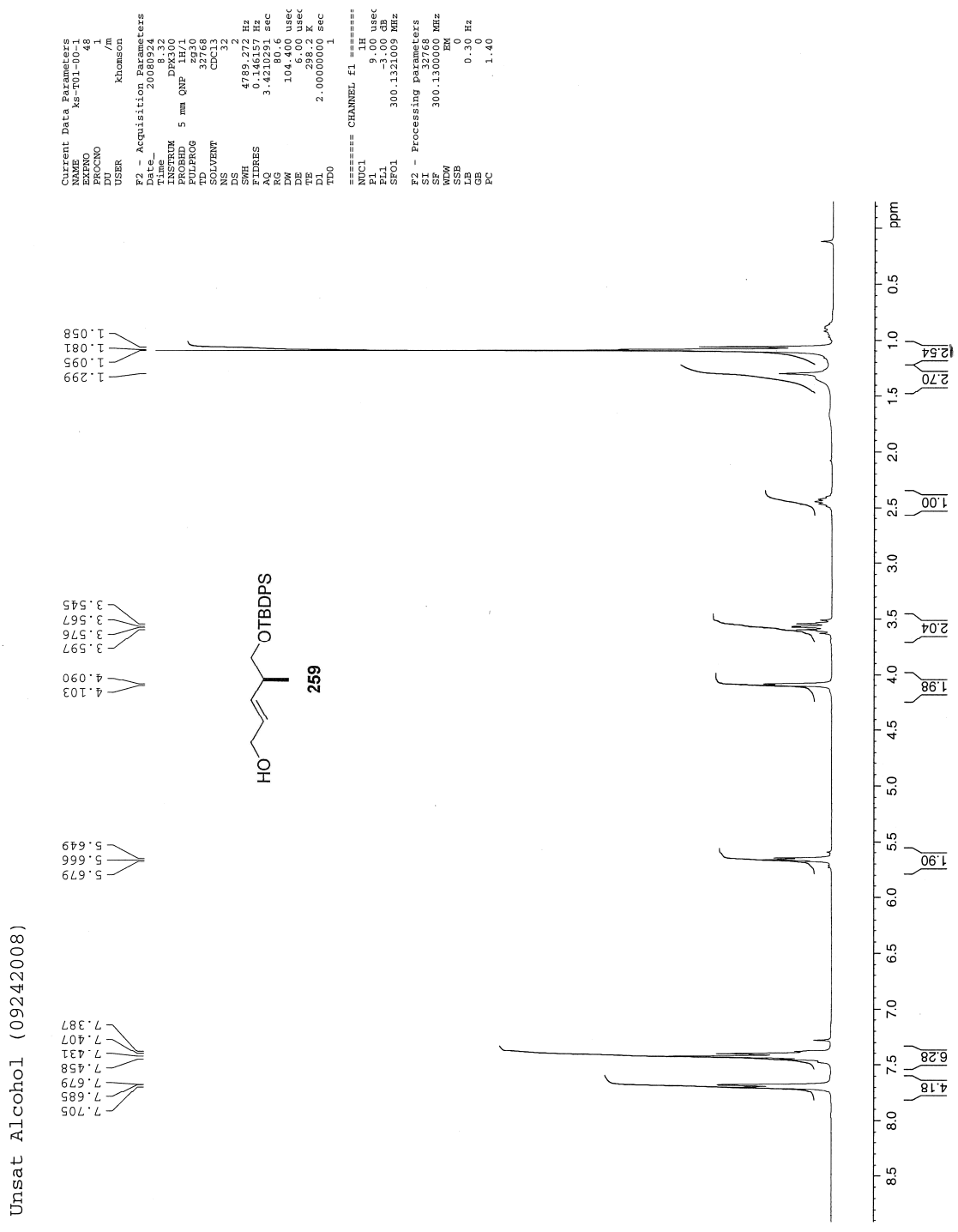

```
Current Data Parameters
NAME         ks-T01-77-1
EXPNO                  4
PROCNO                 1
DU                    /m
USER            khomson

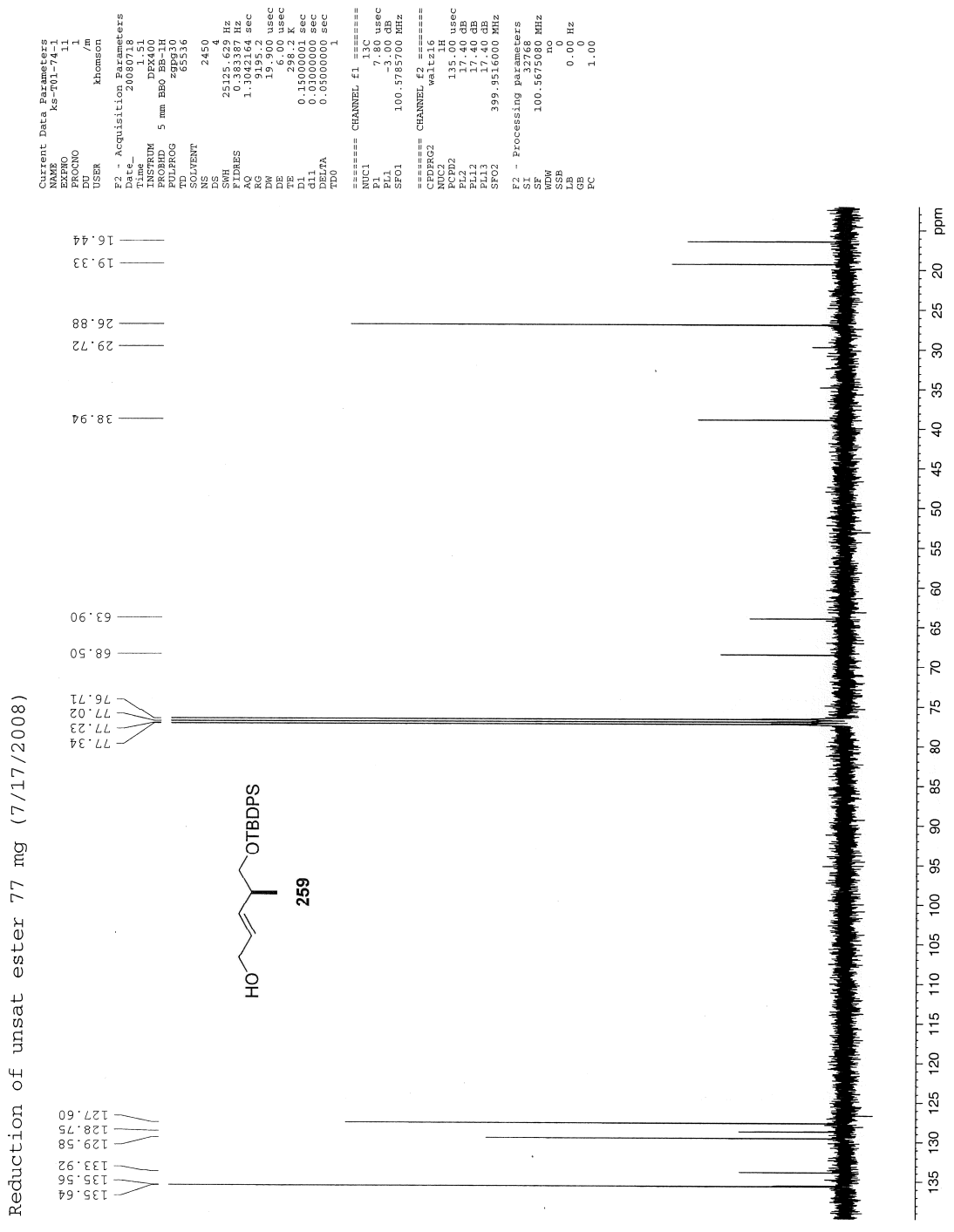
F2 - Acquisition Parameters
Date_           20080714
Time                5.14
INSTRUM          DPX400
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT
NS                 2450
DS                    4
SWH           25125.629 Hz
FIDRES         0.383387 Hz
AQ            1.3042164 sec
RG                16384
DW               19.900 usec
DE                6.00 usec
TE                298.2 K
D1           0.15000001 sec
d11          0.03000000 sec
DELTA        0.05000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   7.80 usec
PL1                 -3.00 dB
SFO1         100.5785700 MHz

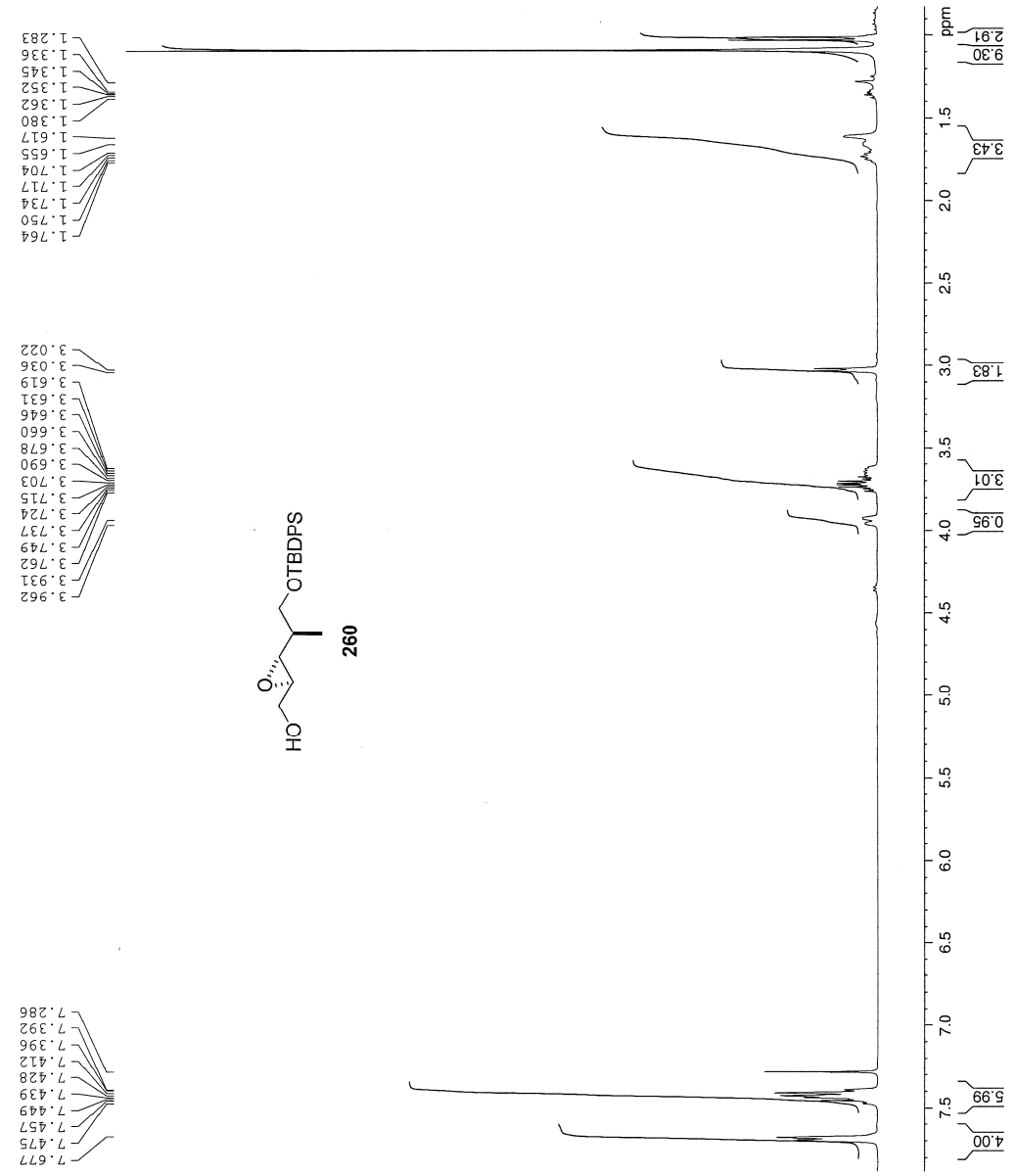
======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              135.00 usec
PL2                 17.40 dB
PL12                17.40 dB
PL13                17.40 dB
SFO2         399.9516000 MHz

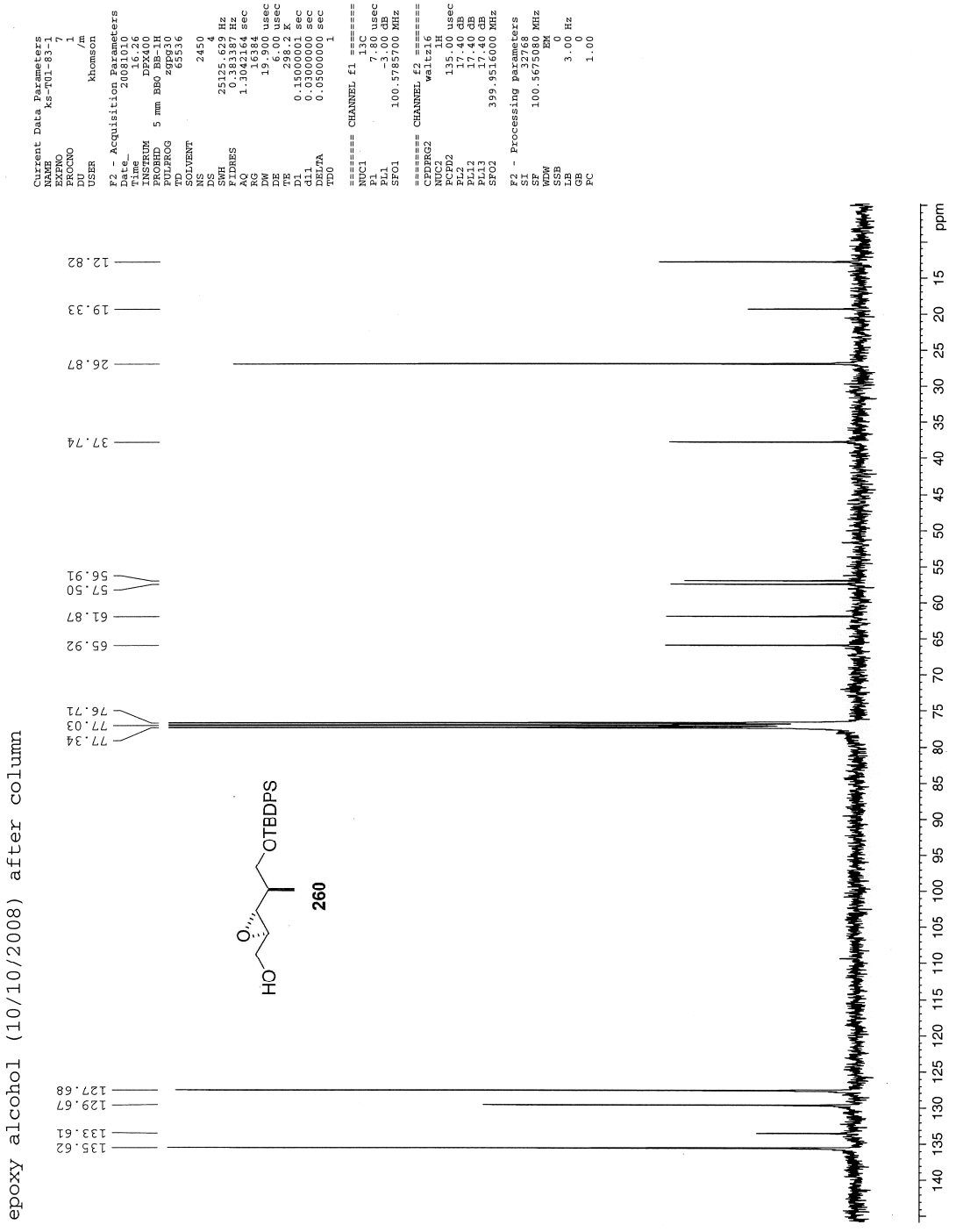
F2 - Processing parameters
SI                 32768
SF           100.5675080 MHz
WDW                   EM
SSB                    0
LB                  3.00 Hz
GB                     0
PC                  1.40
```

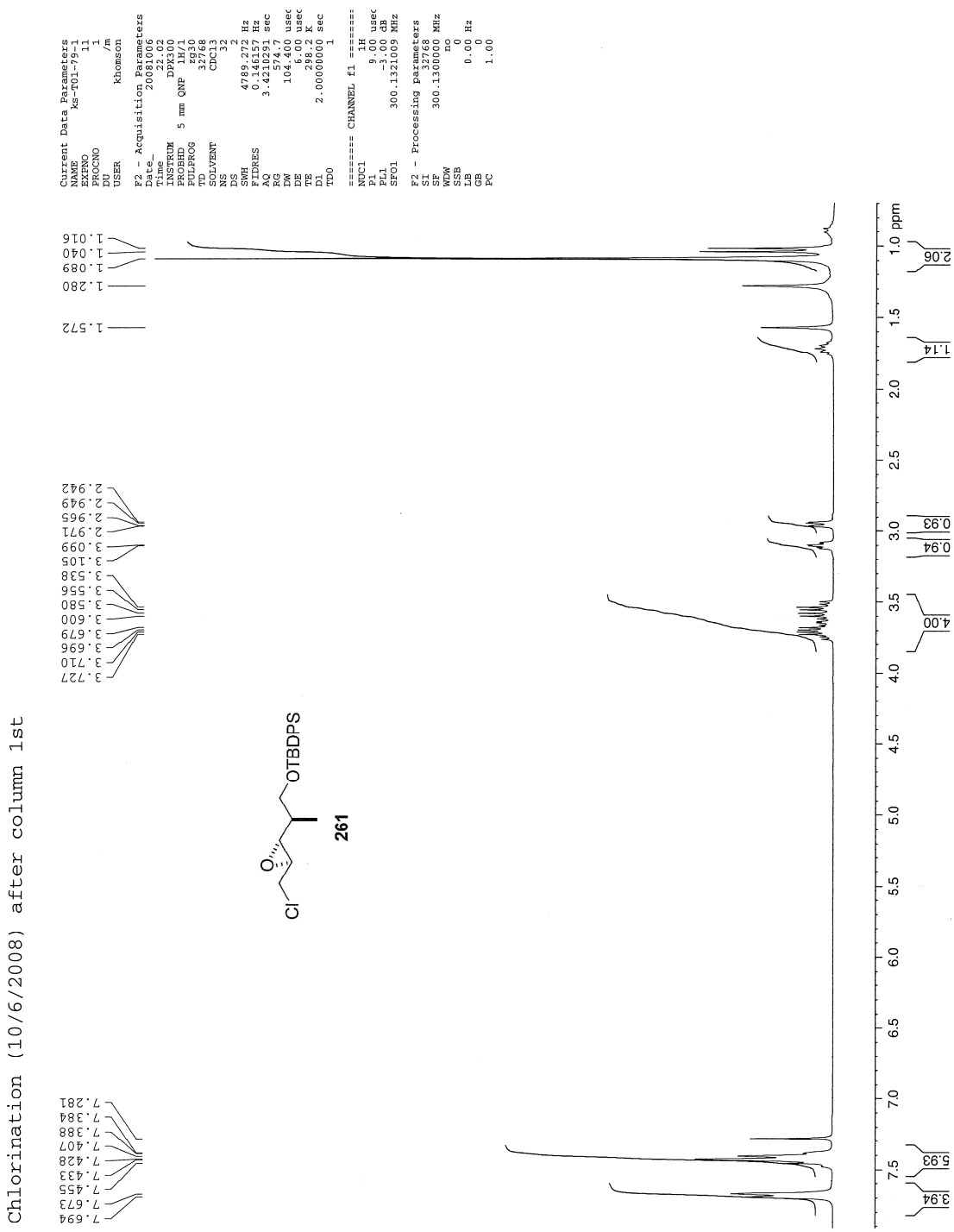

Unsat Alcohol (09242008)
Current Data Parameters
NAME ks-T01-00-1
EXPNO 48
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20080924
Time_ 8.32
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 80.6
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
1.058
1.081
1.095
1.299
3.545
3.567
3.576
3.597
4.090
4.103
5.649
5.666
5.679
7.387
7.407
7.431
7.458
7.679
7.685
7.705
HO
OTBDPS
259
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
12.54
2.70
1.00
2.04
1.98
1.90
6.28
4.18

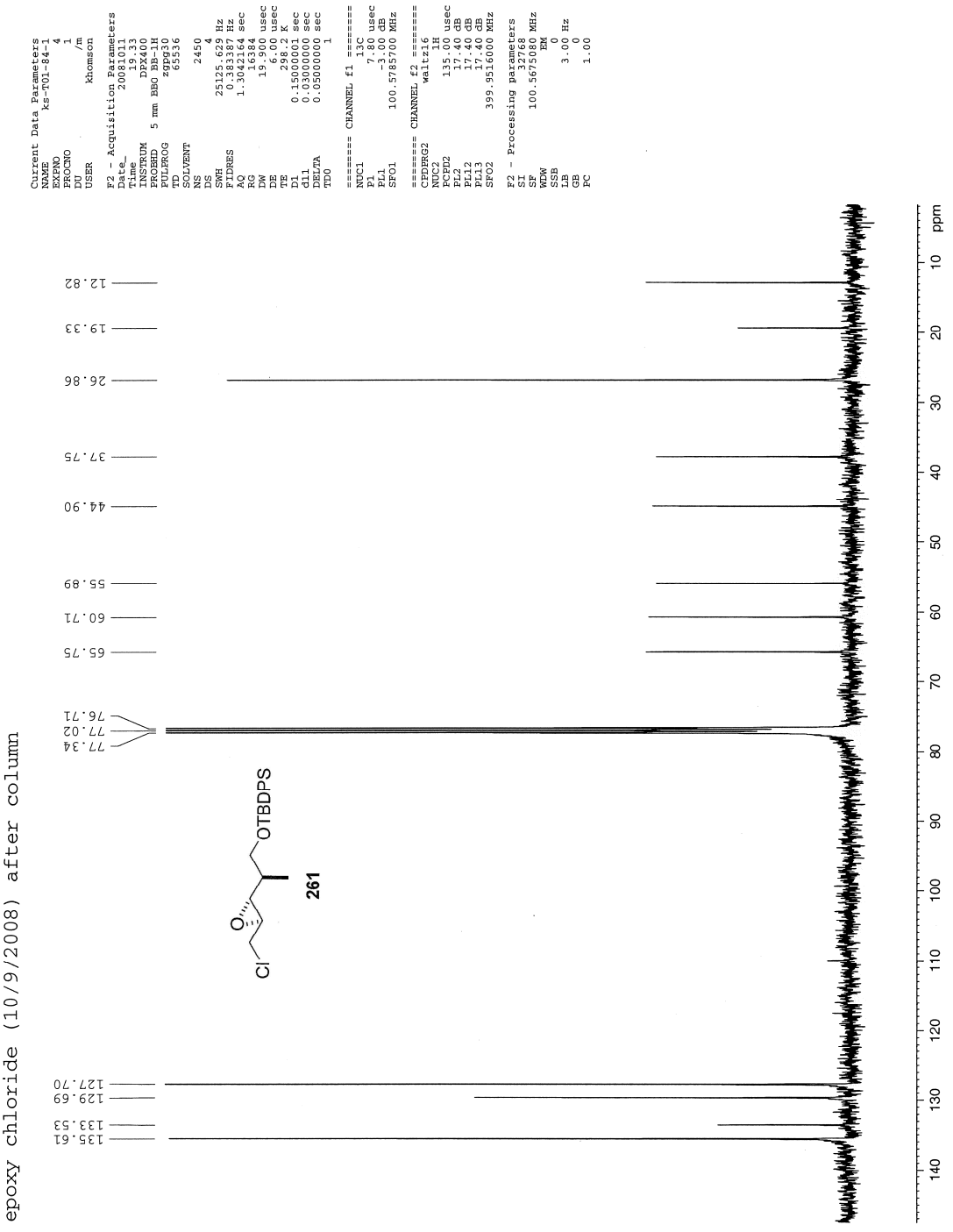

Reduction of unsat ester 77 mg (7/17/2008)
HO
OTBDPS
259
16.44
19.33
26.88
29.72
38.94
63.90
68.50
76.71
77.02
77.23
77.34
127.60
128.75
129.58
133.92
135.56
135.64
ppm

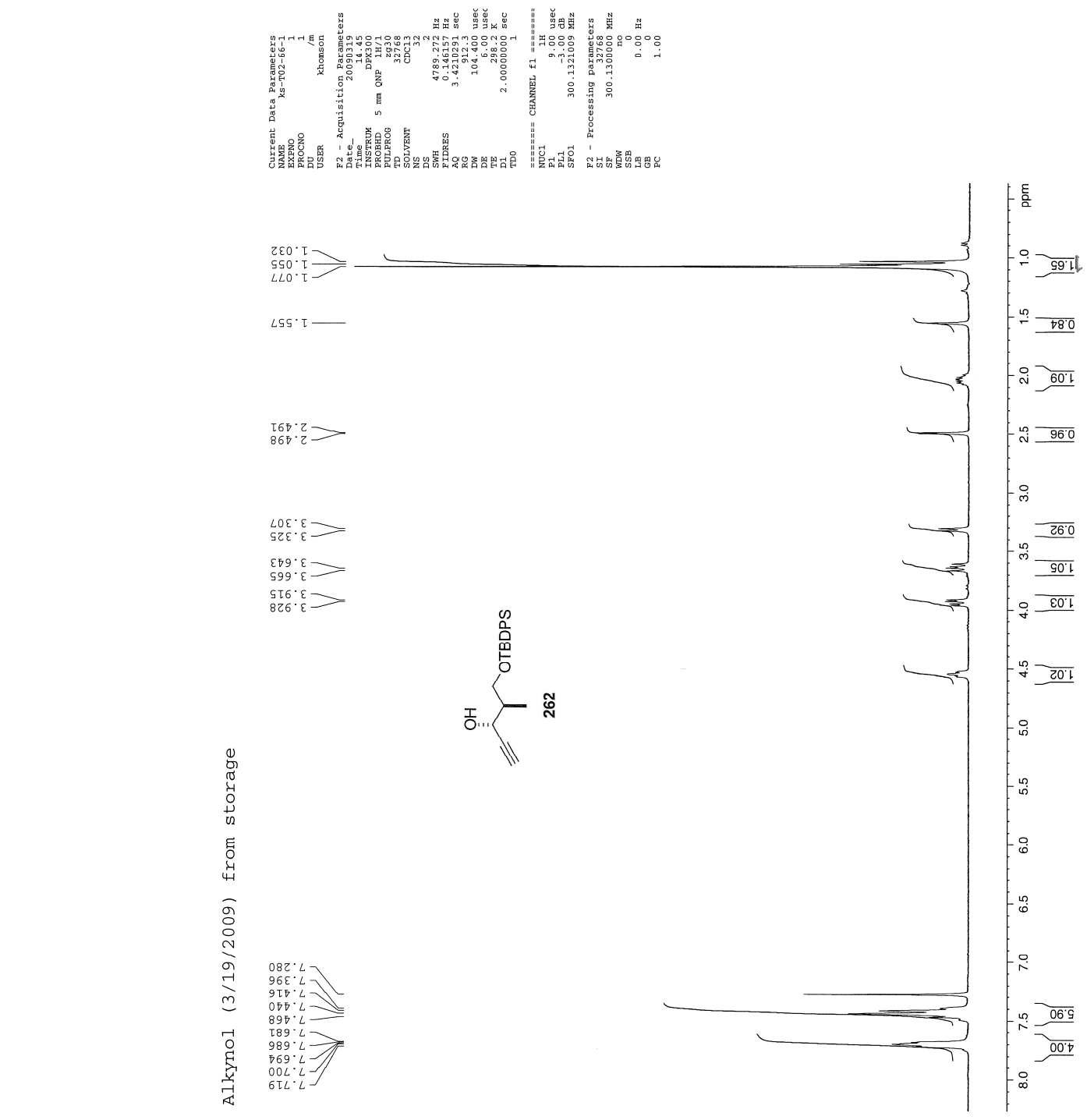
epoxy alcohol (10/10/2008) after column

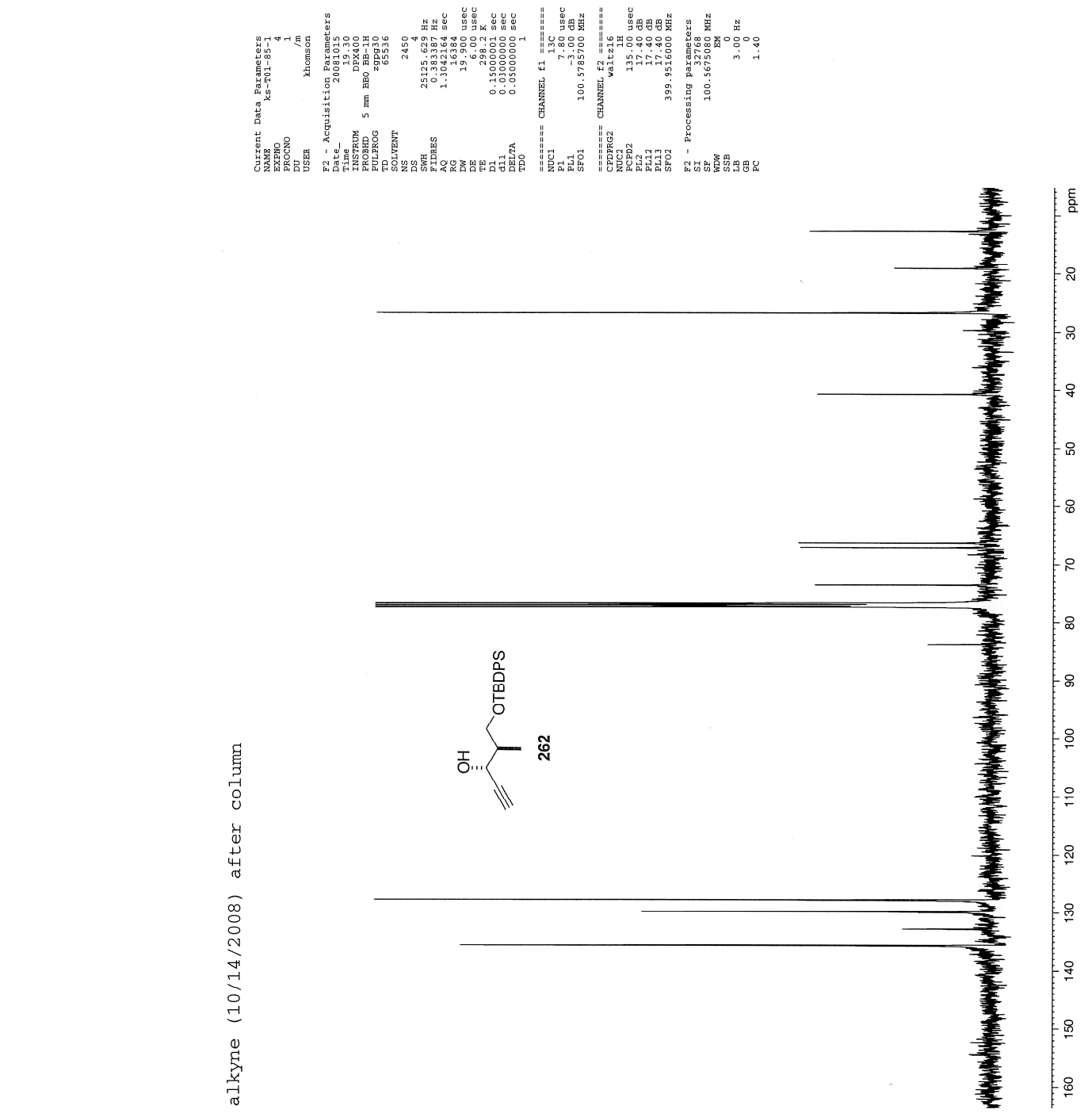


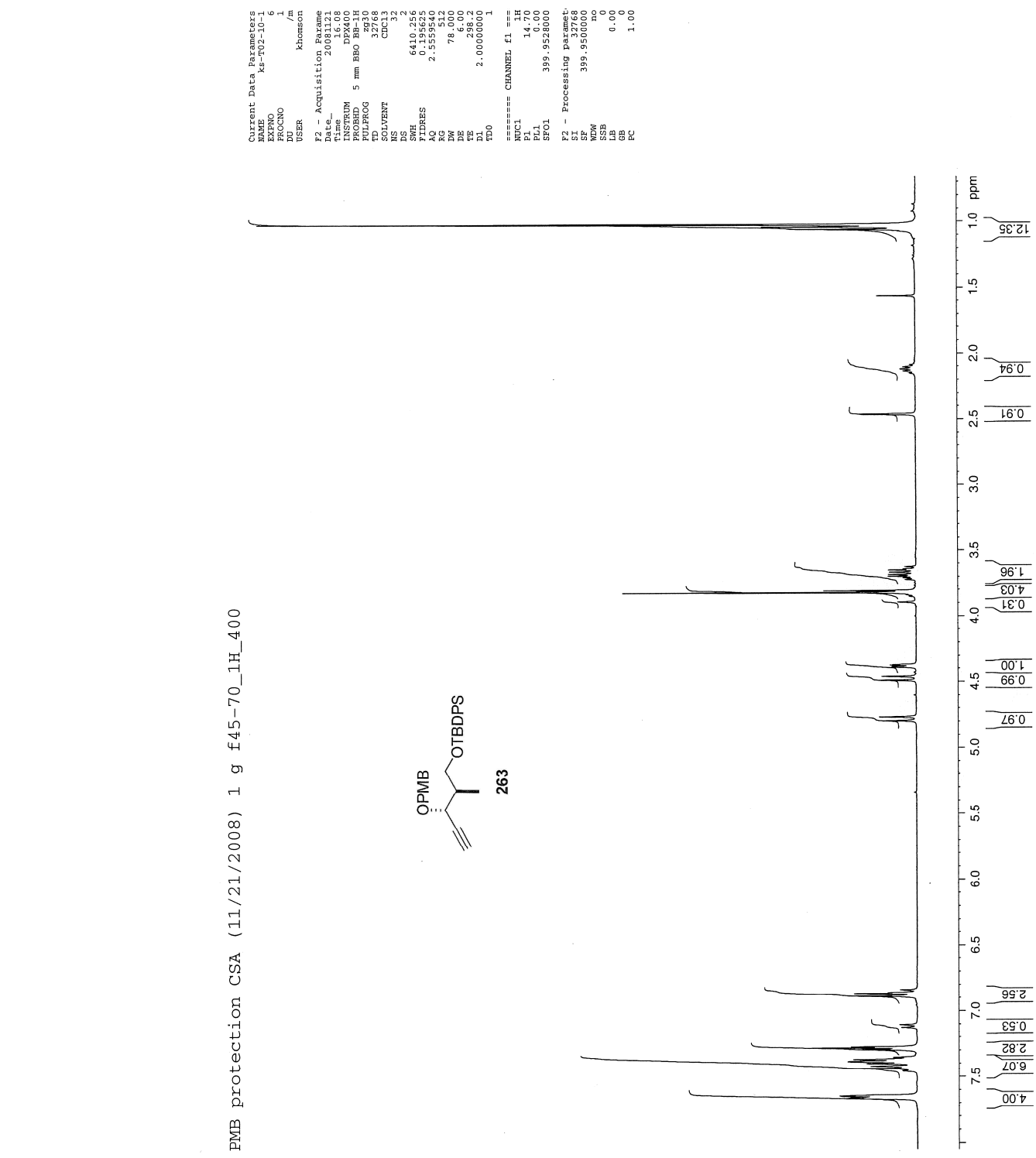

epoxy alcohol (10/10/2008) after column
Current Data Parameters
NAME ks-T01-83-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20081010
Time 16.26
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.30421164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.60 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
135.62
133.61
129.67
127.68
77.34
77.03
76.71
65.92
61.87
57.50
56.91
37.74
26.87
19.33
12.82
OTBDPS
HO
260
ppm

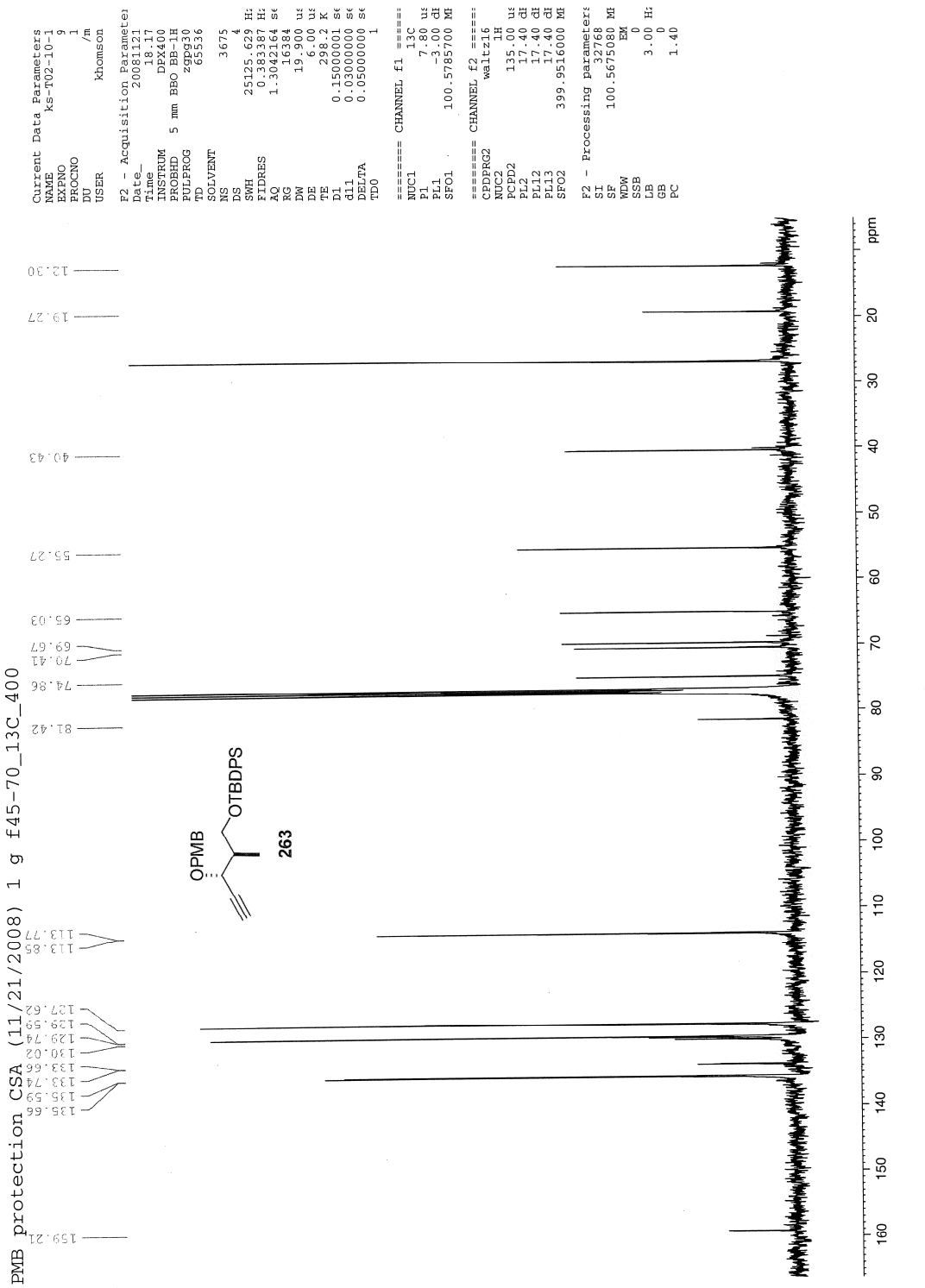

Chlorination (10/6/2008) after column 1st
Current Data Parameters
NAME ks-f01-79-1
EXPNO 11
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20081006
Time 22.02
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OTBDPS
Cl
261
ppm

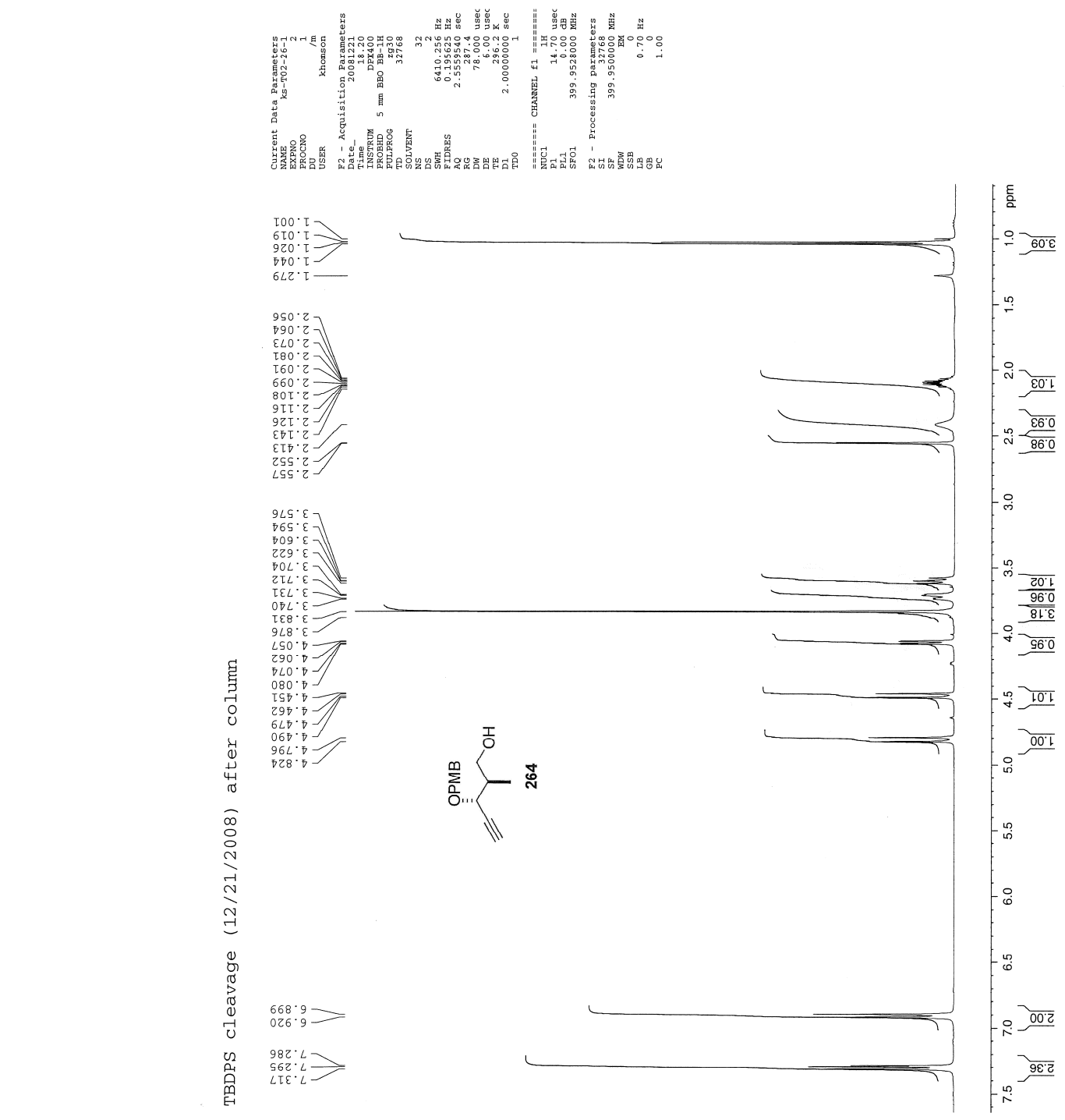

epoxy chloride (10/9/2008) after column
Current Data Parameters
NAME ks-T01-84-1
EXPNO 4
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20081011
Time 19.33
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.30421164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
135.61
133.53
129.69
127.70
77.34
77.02
76.71
65.75
60.71
55.89
44.90
37.75
26.86
19.33
12.82
OTBDPS
Cl
261
ppm

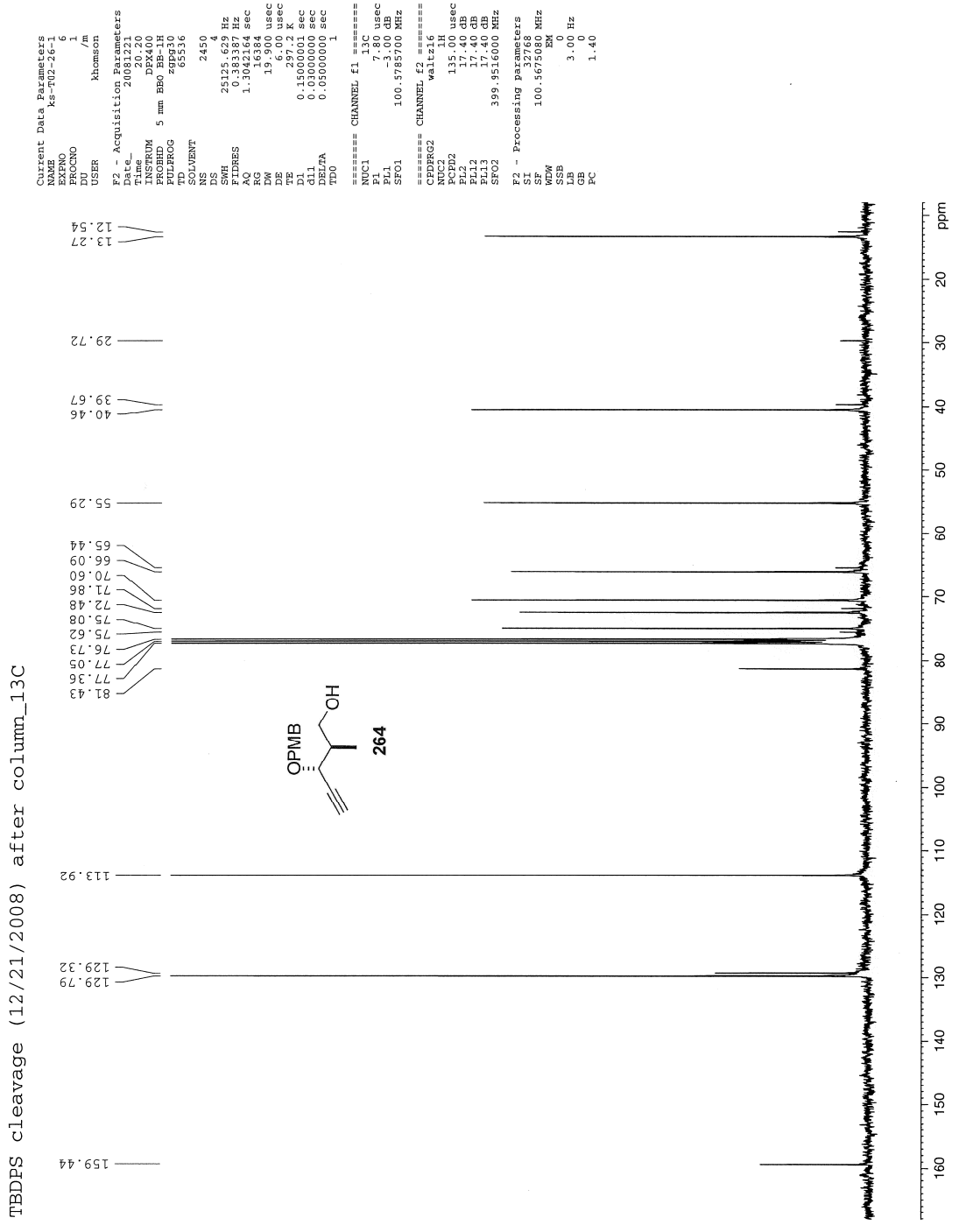

Alkynol (3/19/2009) from storage
Current Data Parameters
NAME ks-t02-66-1
EXPNO 1
PROCNO 1
DU /m
USER khomson
P2 - Acquisition Parameters
Date_ 20090319
Time 11.45
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102291 sec
RG 912.3
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
P2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.719
7.700
7.694
7.686
7.681
7.468
7.440
7.416
7.396
7.280
3.928
3.915
3.665
3.643
3.325
3.307
2.498
2.491
1.557
1.077
1.055
1.032
OH
OTBDPS
262
ppm
4.00
5.90
1.02
1.03
1.05
0.92
0.96
1.09
0.84
1.65

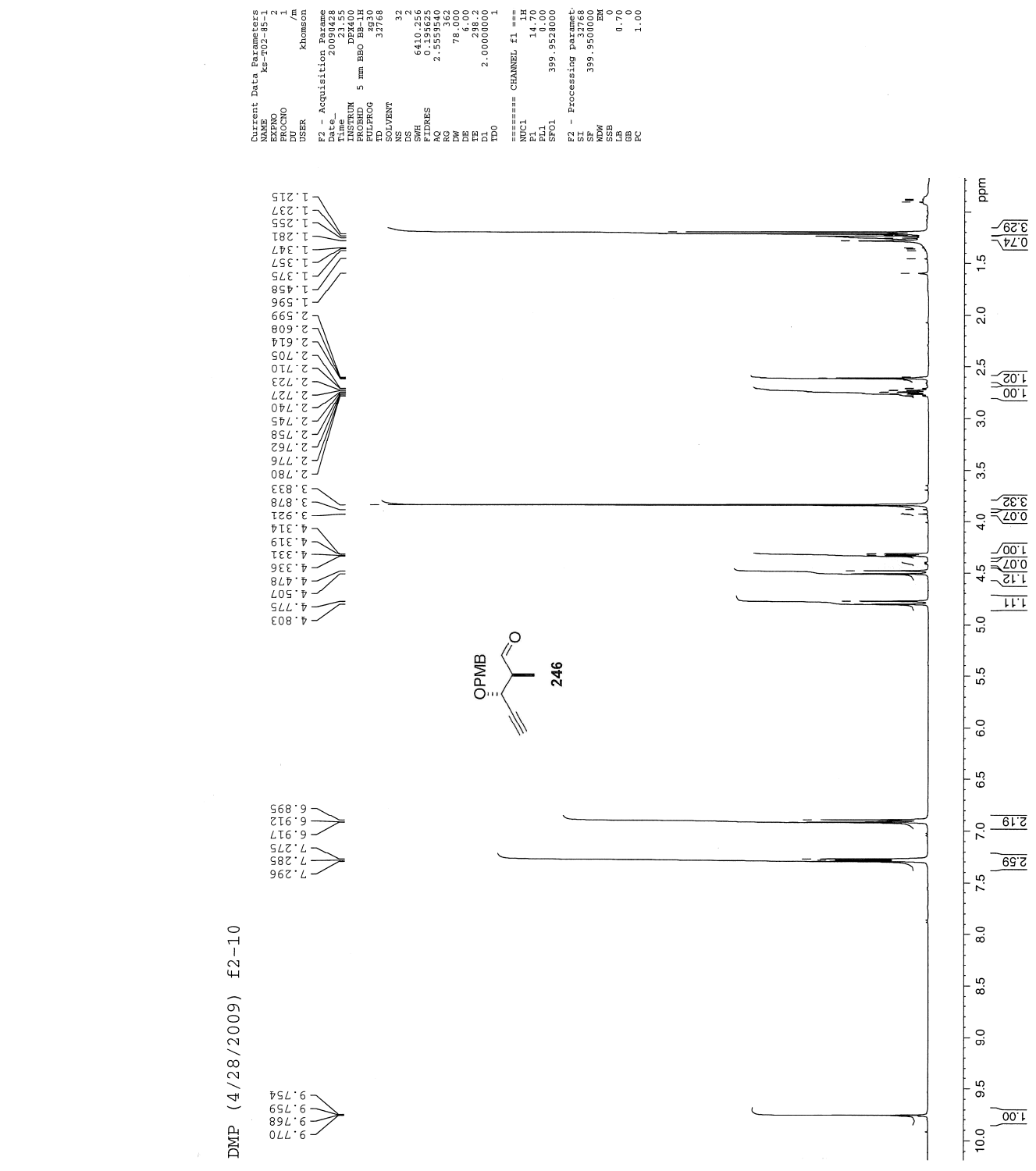

alkyne (10/14/2008) after column
Current Data Parameters
NAME ks-T01-85-1
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081015
Time 19.30
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675060 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OH
OTBDPS
262
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

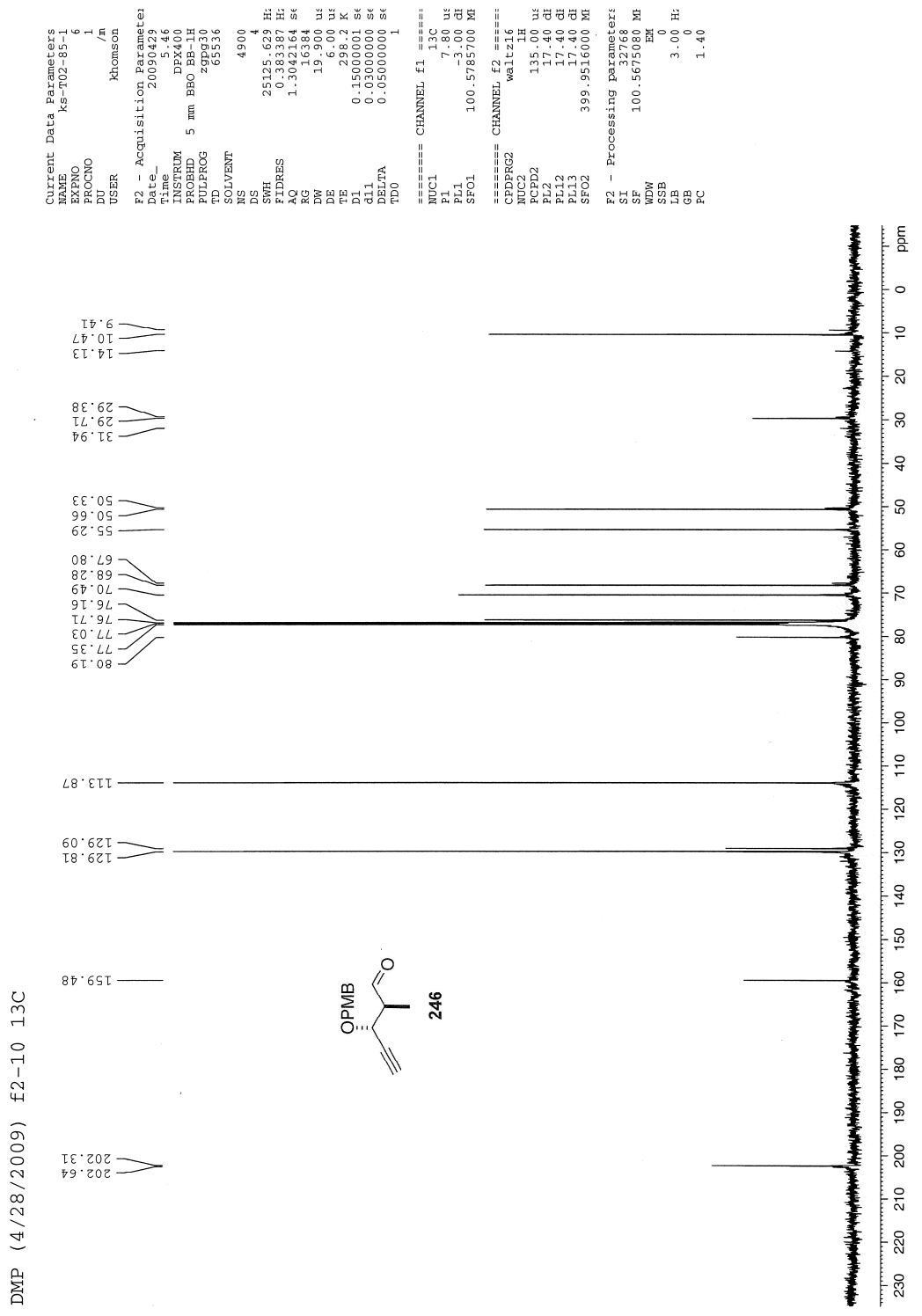

PMB protection CSA (11/21/2008) 1 g f45-70_1H_400
Current Data Parameters
NAME ks-T02-10-1
EXPNO 6
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parame
Date_ 20081121
Time 16.08
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 512
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing paramet
SI 32768
SF 399.9500000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.00
OPMB
OTBDPS
263
4.00
6.07
2.82
0.53
2.56
0.97
1.00
0.99
0.31
4.03
1.96
0.91
0.94
12.35
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

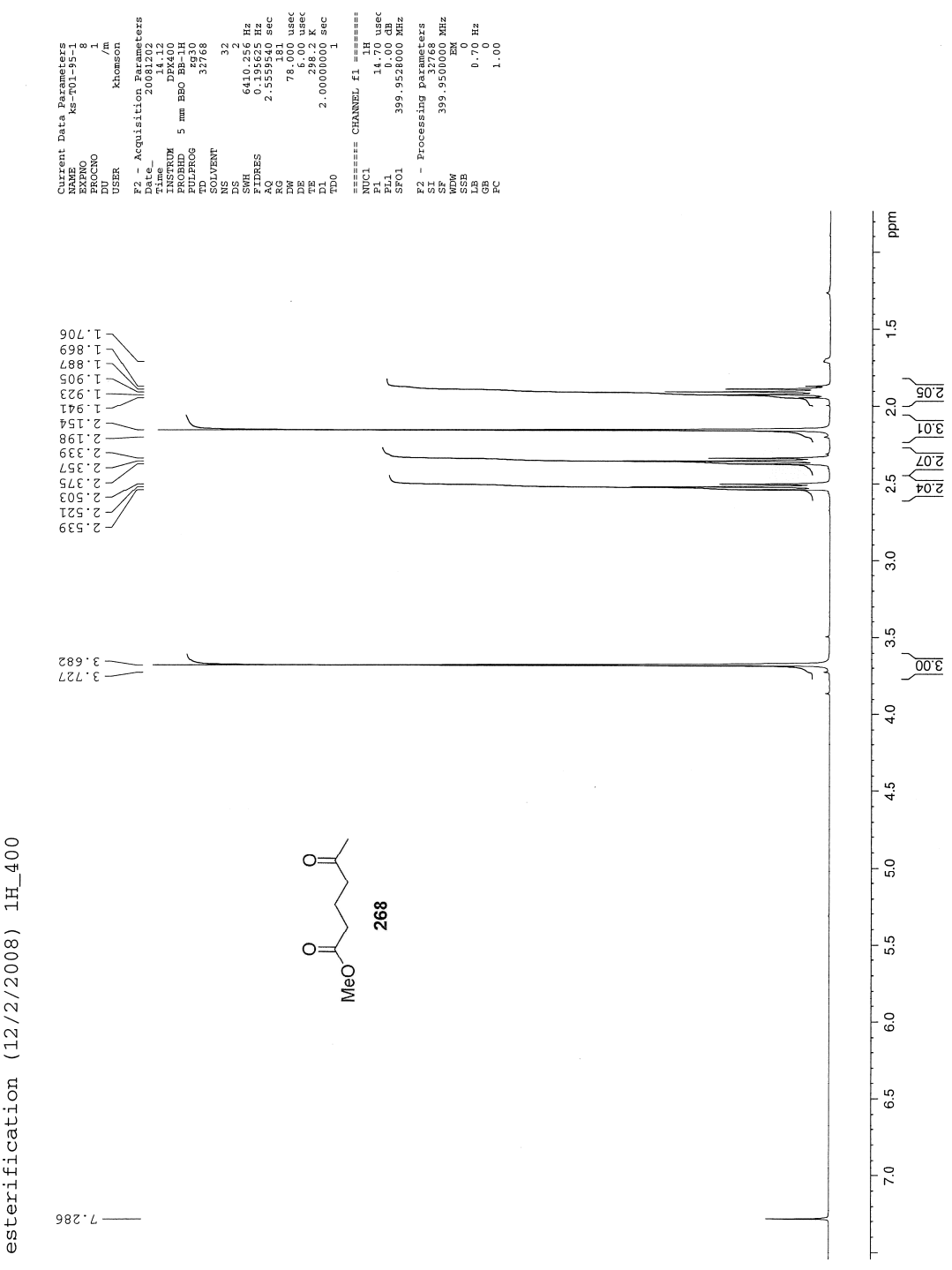

PMB protection CSA (11/21/2008) 1 g f45-70_13C_400
Current Data Parameters
NAME ks-T02-10-1
EXPNO 9
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20081121
Time 18.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 3675
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
OPMB
OTBDPS
263
159.21
135.66
135.59
133.74
133.66
130.02
129.74
129.59
127.62
113.85
113.77
81.42
74.86
70.41
69.67
65.03
55.27
40.43
19.27
12.30
ppm

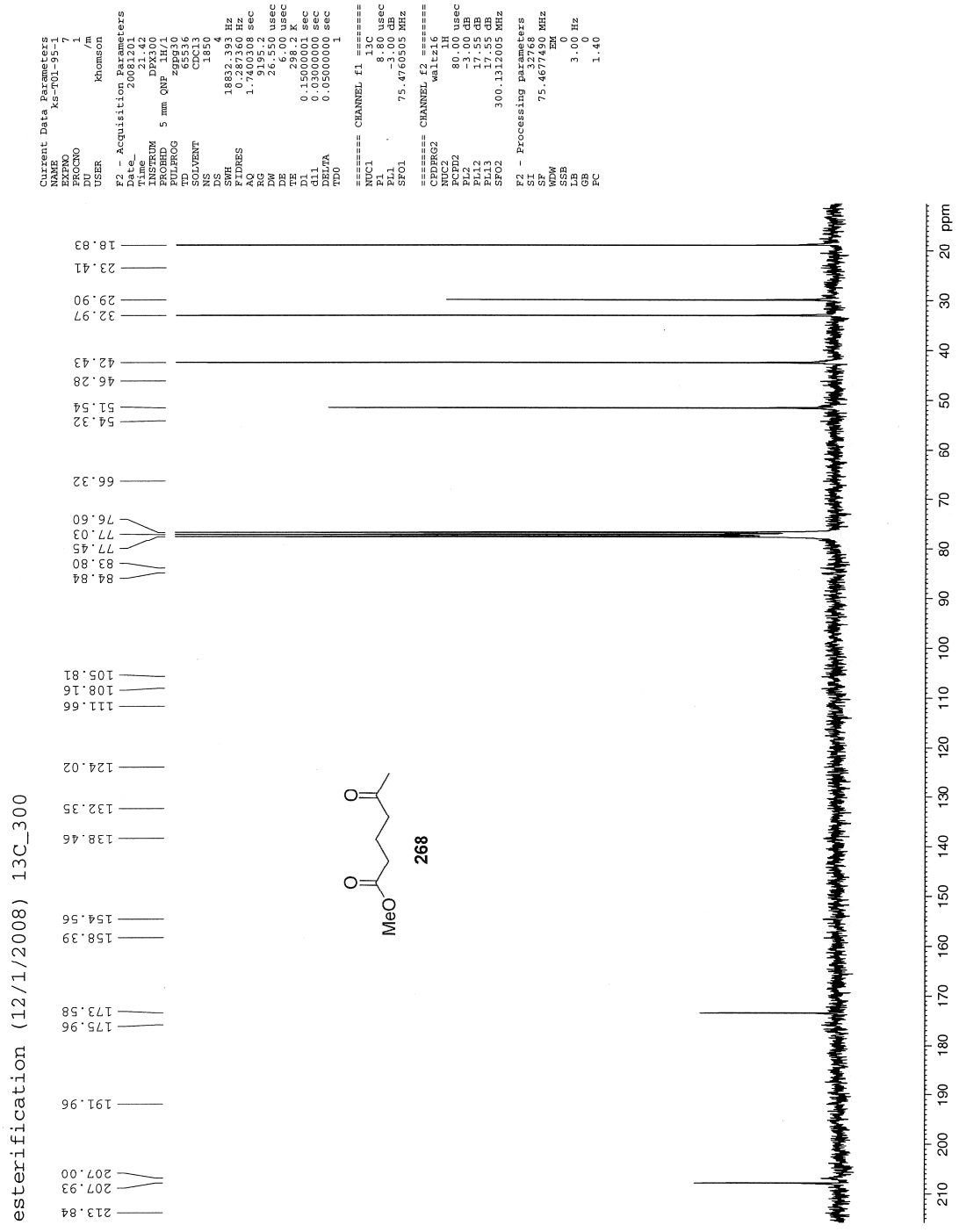

TBDPS cleavage (12/21/2008) after column
Current Data Parameters
NAME ks-T02-26-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20081221
Time 14.20
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 287.4
DW 78.000 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OPMB
OH
264
ppm
3.09
1.03
0.93
0.98
1.02
0.96
3.18
0.95
1.01
1.00
2.00
2.36

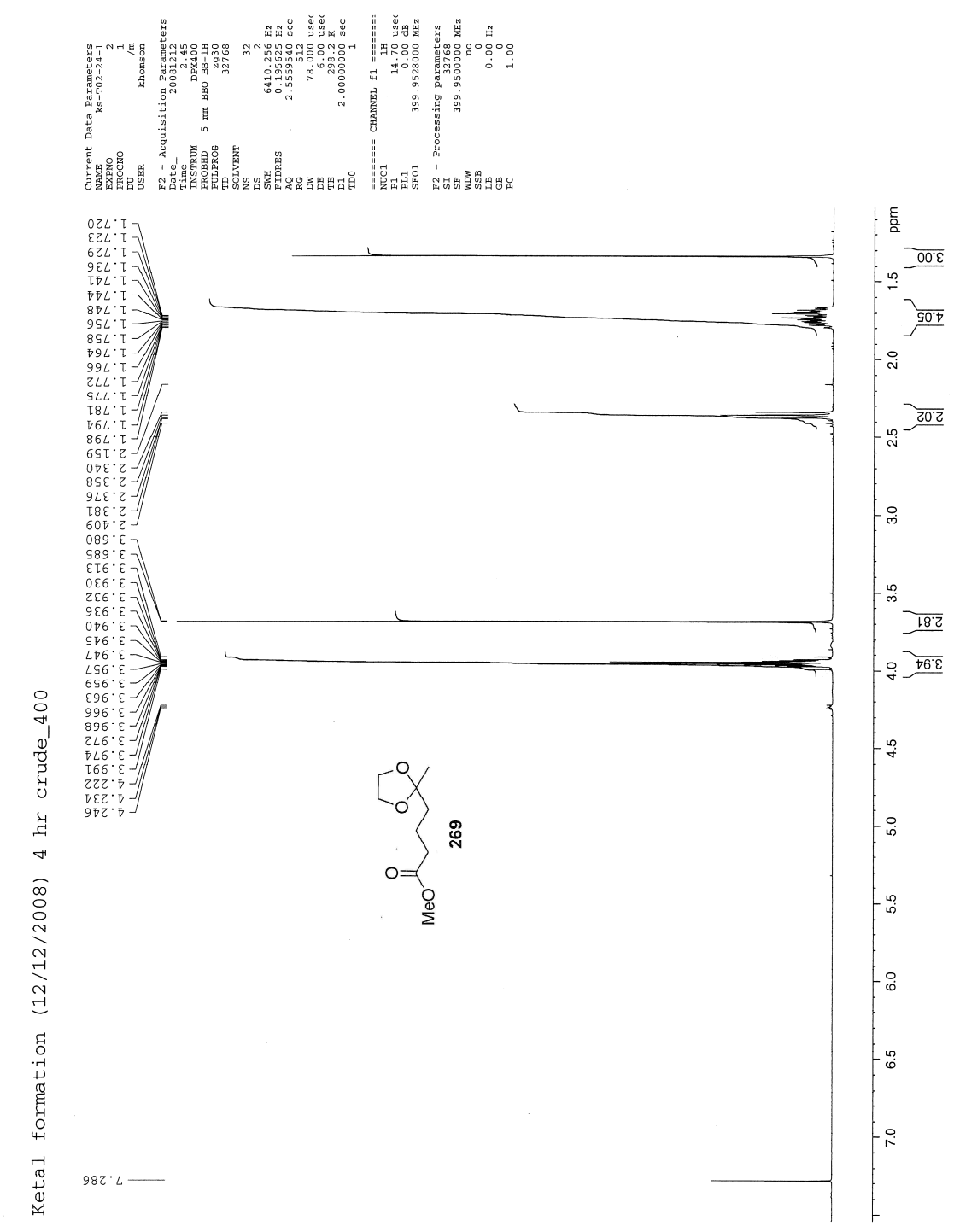

TBDPS cleavage (12/21/2008) after column_13C
Current Data Parameters
NAME ks-T02-26-1
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081221
Time 20.20
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.30421164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 297.2 K
D1 0.15000001 sec
D11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675040 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OPMB
OH
264
ppm

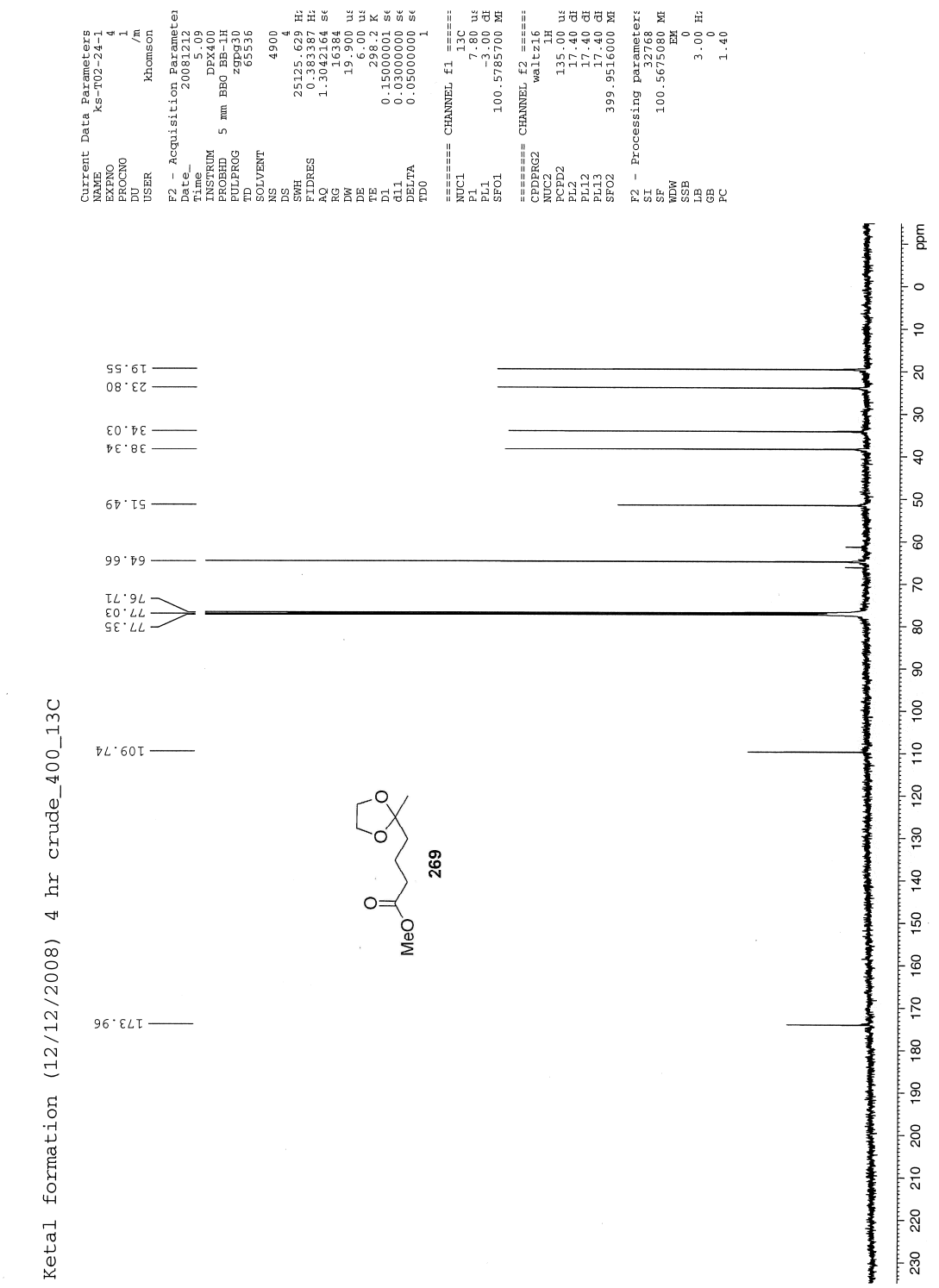

DMP (4/28/2009) f2-10
Current Data Parameters
NAME ks-T02-85-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parame
Date_ 20090428
Time 23.55
INSTRUN DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 362
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TDO 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing paramet
SI 32768
SF 399.9500000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
OPMB
246
ppm


DMP (4/28/2009) f2-10 13C
Current Data Parameters
NAME ks-TO2-85-1
EXPNO 6
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20090429
Time_ 5.46
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 4900
DS 4
SWH 25125.629 H
FIDRES 0.3833387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
OPMB
246
202.64
202.31
159.48
129.81
129.09
113.87
80.19
77.35
77.03
76.71
76.16
70.49
68.28
67.80
55.29
50.66
50.33
31.94
29.71
29.38
14.13
10.47
9.41
ppm

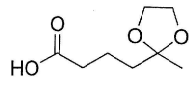

esterification (12/2/2008) 1H_400
Current Data Parameters
NAME ks-T01-95-1
EXPNO 8
PROCNO 1
DU /m
USER khomson
P2 - Acquisition Parameters
Date_ 20081202
Time_ 14.12
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
7.286
3.727
3.682
2.539
2.521
2.503
2.375
2.357
2.339
2.198
2.154
1.941
1.923
1.905
1.887
1.869
1.706
3.00
2.04
2.07
3.01
2.05
O
O
MeO
268
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5


esterification (12/1/2008) 13C_300
Current Data Parameters
NAME ks-T01-95-1
EXPNO 7
PROCNO 1
USER khomson
F2 - Acquisition Parameters
Date_ 20081201
Time 21.42
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1850
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.74400308 sec
RG 9195.2
DW 26.550 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -3.00 dB
SFO1 75.4760505 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 3.00 dB
PL12 17.55 dB
PL13 17.55 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
18.83
23.41
29.90
32.97
42.43
46.28
51.54
54.32
66.32
76.60
77.03
77.45
83.80
84.84
105.81
108.16
111.66
124.02
132.35
138.46
154.56
158.39
173.58
175.96
191.96
207.00
207.93
213.84
O
O
MeO
268
ppm


Ketal formation (12/12/2008) 4 hr crude_400
Current Data Parameters
NAME ks-T02-24-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20081212
Time 14.45
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 27766
SF 199.9500000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
269
MeO
7.286
4.246
4.234
4.222
3.991
3.974
3.972
3.968
3.966
3.963
3.959
3.957
3.947
3.945
3.940
3.936
3.932
3.930
3.913
3.685
3.680
2.409
2.381
2.376
2.358
2.340
2.159
1.798
1.794
1.781
1.775
1.772
1.766
1.764
1.758
1.756
1.748
1.744
1.741
1.736
1.729
1.723
1.720
3.00
4.05
2.02
2.81
3.94
ppm


Ketal formation (12/12/2008) 4 hr crude_400_13C
Current Data Parameters
NAME ks-TO2-24-1
EXPNO 4
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20081212
Time_ 5.09
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 4900
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
19.55
23.80
34.03
38.34
51.49
64.66
76.71
77.03
77.35
109.74
173.96
MeO
269
ppm

Hydrolysis (12/1/2008) 1H_400



270


```
Current Data Parameters
NAME          ks-T02-14-1
EXPNO                   2
PROCNO                  1
DU                     /m
USER             khomson

F2 - Acquisition Parame
Date_           20081201
Time               18.17
INSTRUM          DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 32768
SOLVENT
NS                    32
DS                     2
SWH              6410.256
FIDRES          0.195625
AQ              2.5559540
RG                   512
DW                78.000
DE                  6.00
TE                298.2
D1             2.00000000
TD0                    1

======== CHANNEL f1 ===
NUC1                  1H
P1                 14.70
PL1                 0.00
SFO1         399.9528000

F2 - Processing paramet
SI                 32768
SF           399.9500000
WDW                   EM
SSB                    0
LB                  0.70
GB                     0
PC                  1.00
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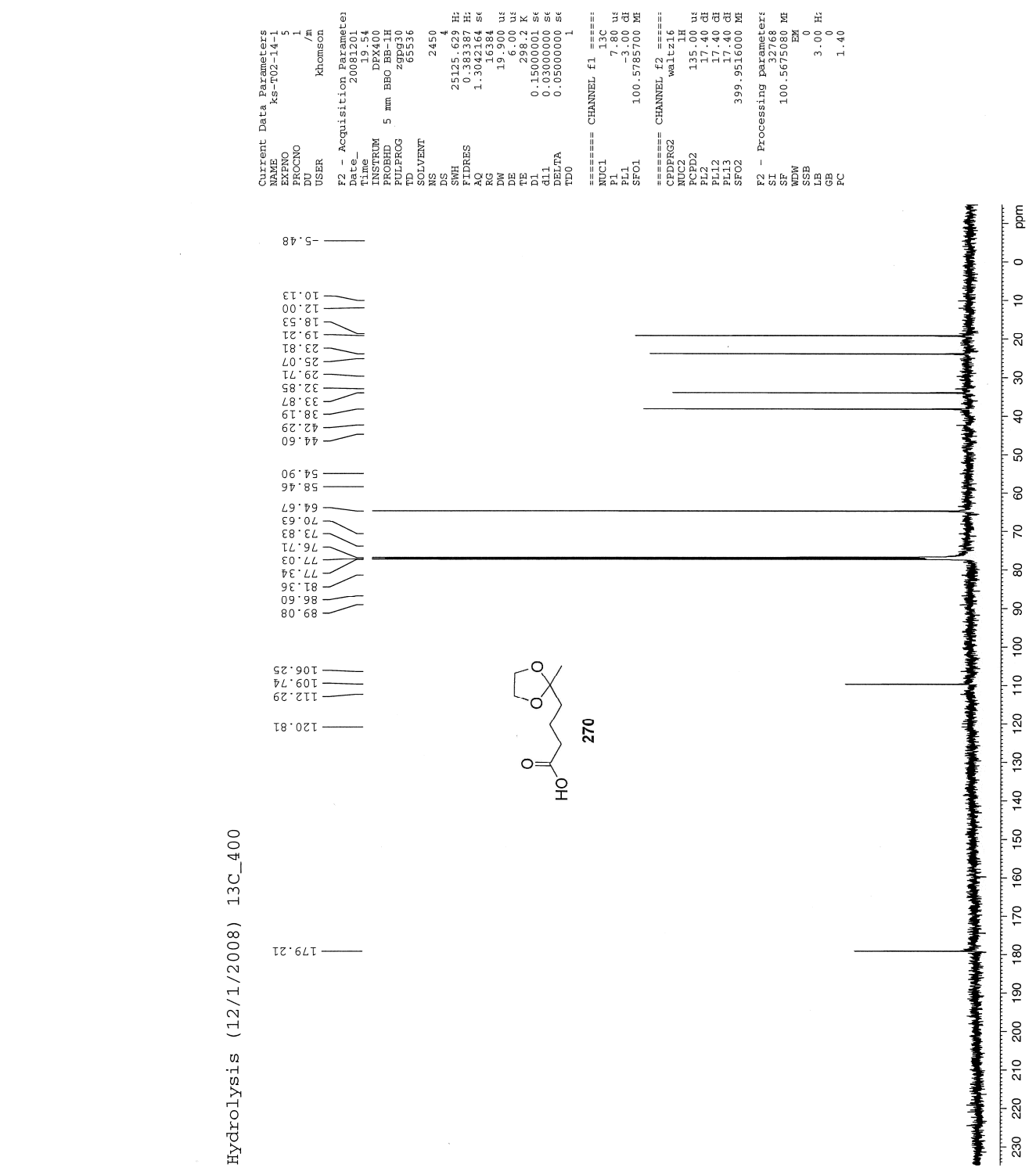
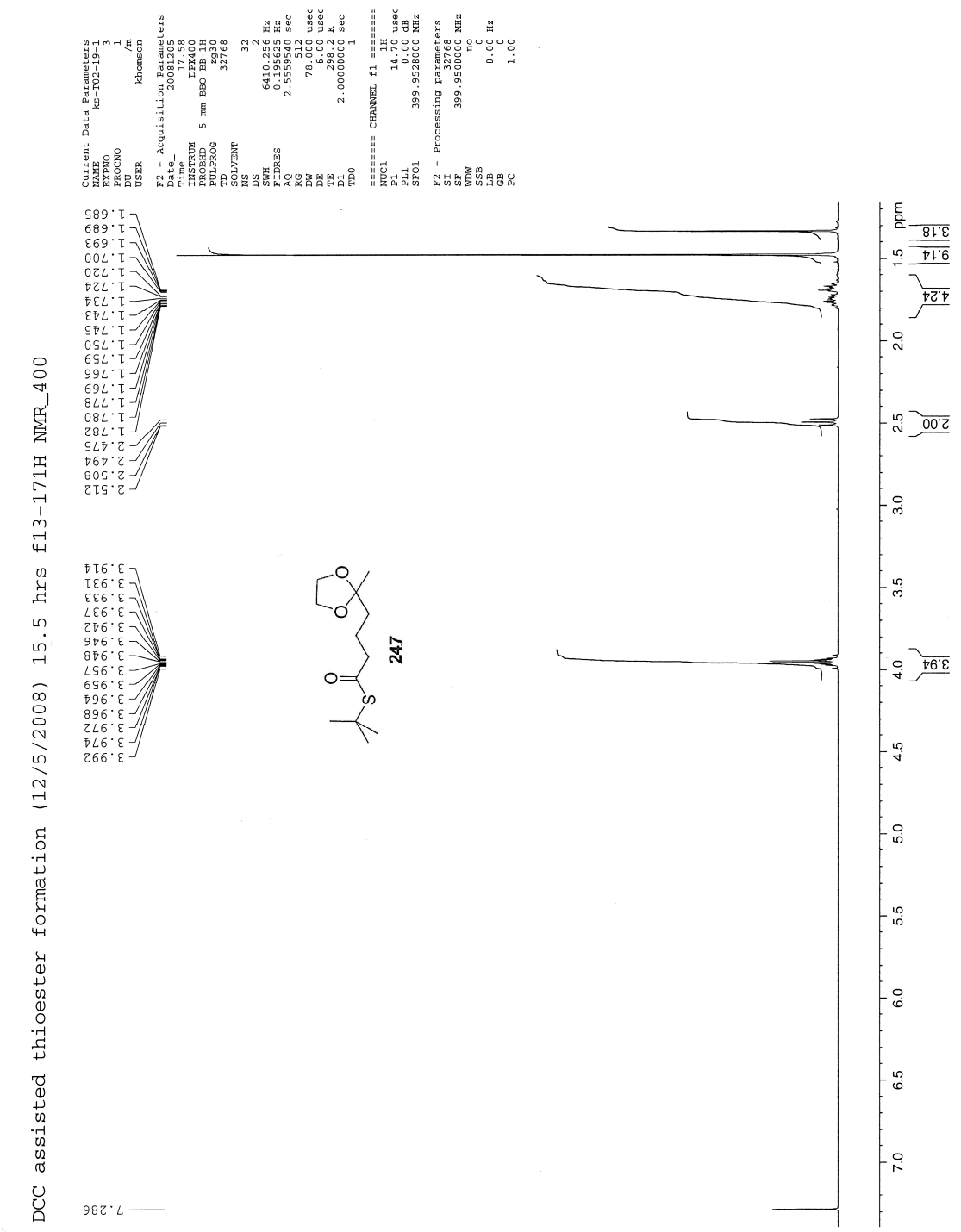
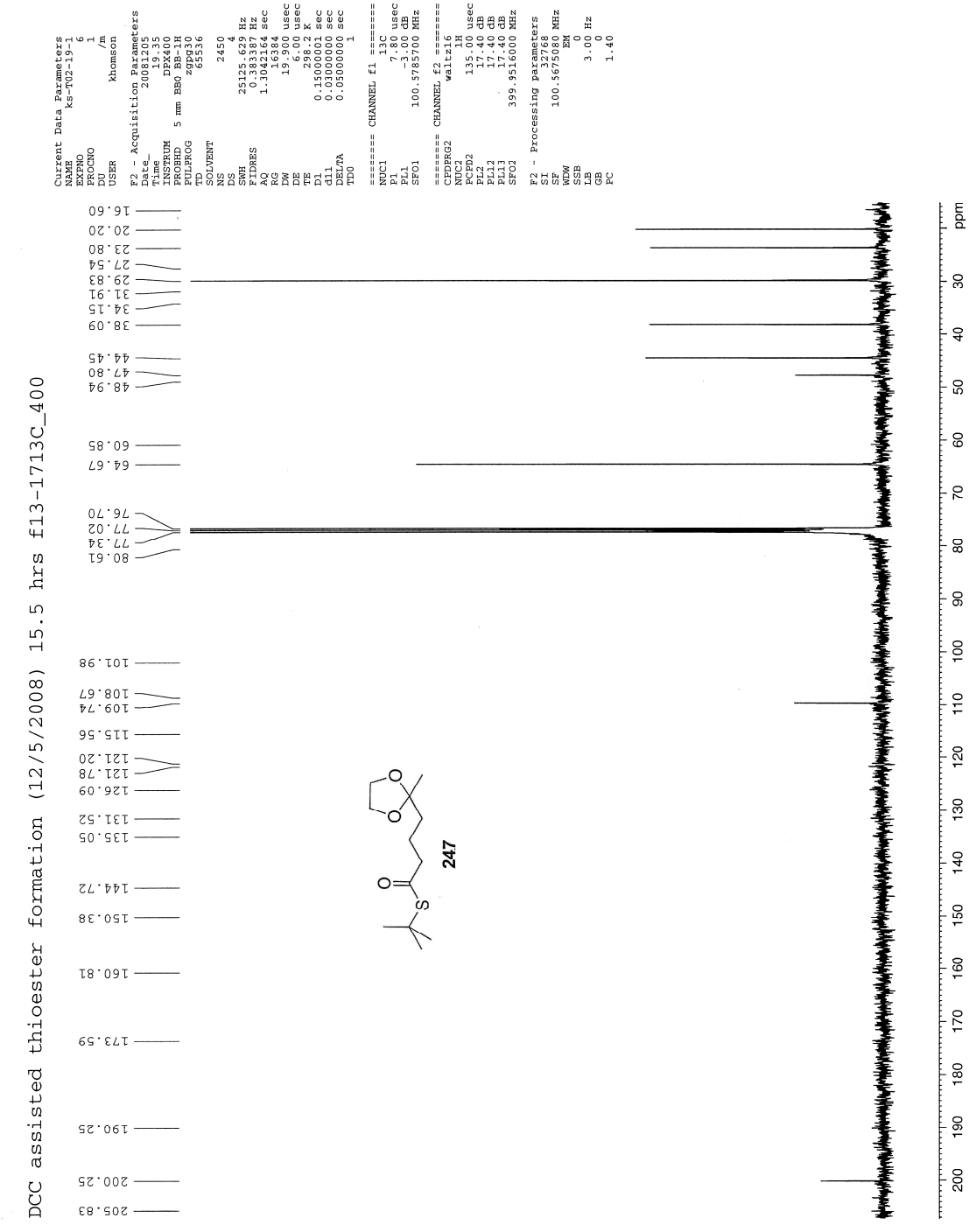
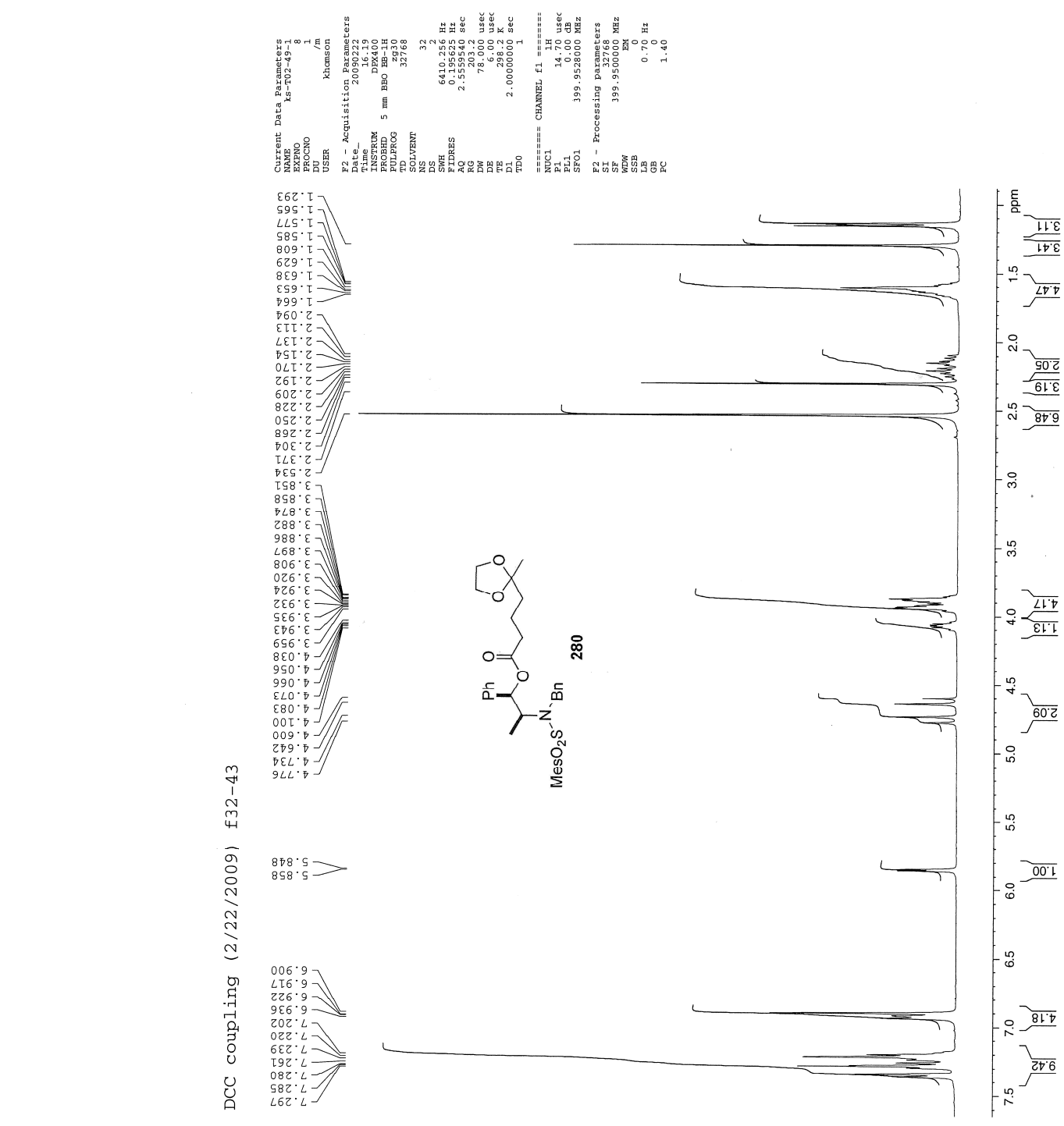
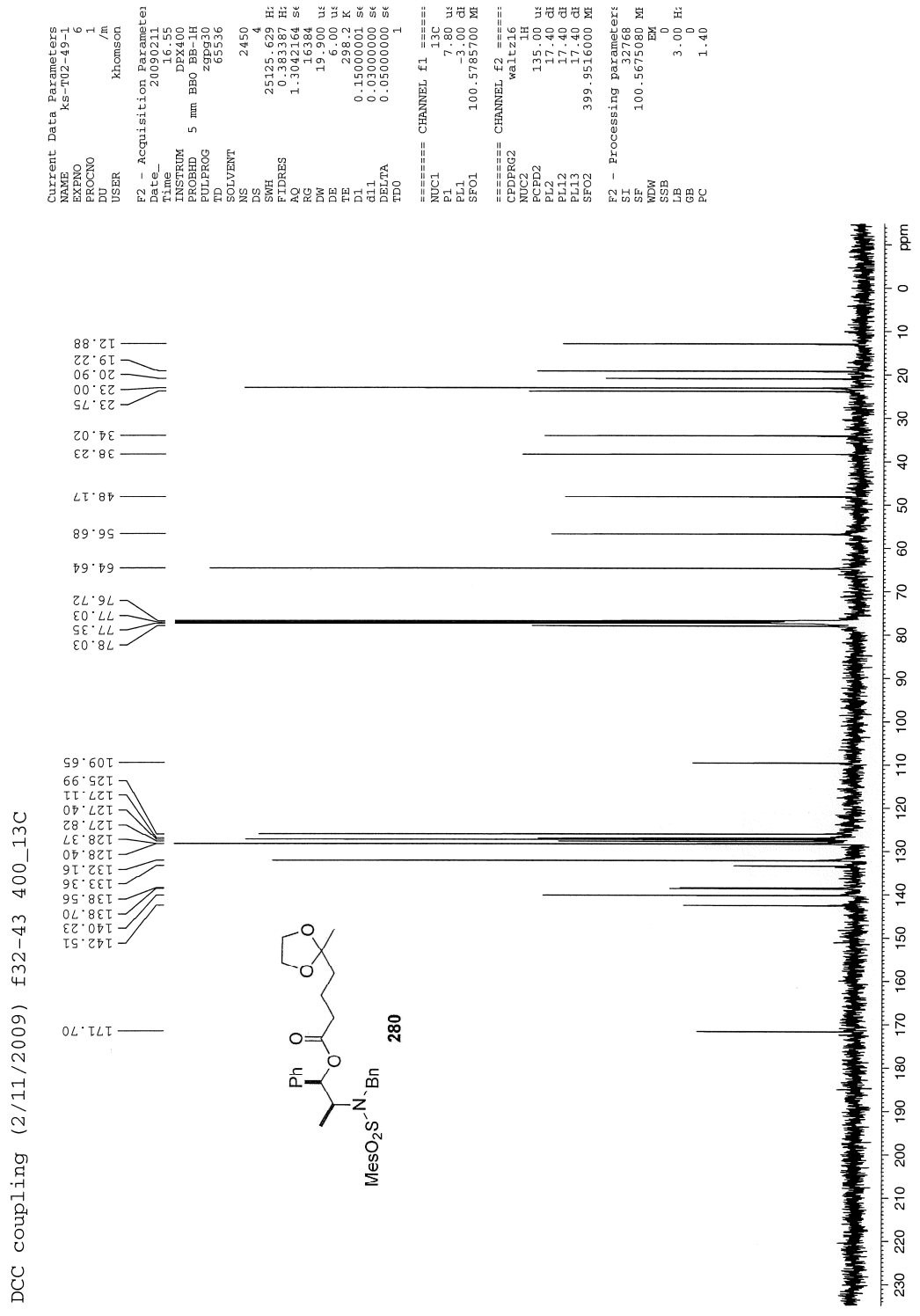

Hydrolysis (12/1/2008) 13C_400
Current Data Parameters
NAME ks-T02-14-1
EXPNO 5
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20081201
Time 19.54
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
-5.48
10.13
12.00
18.53
19.21
23.81
25.07
29.71
32.85
33.87
38.19
42.29
44.60
54.90
58.46
64.67
70.63
73.83
76.71
77.03
77.34
81.36
86.60
89.08
106.25
109.74
112.29
120.81
179.21
270
HO
O
O
O
ppm

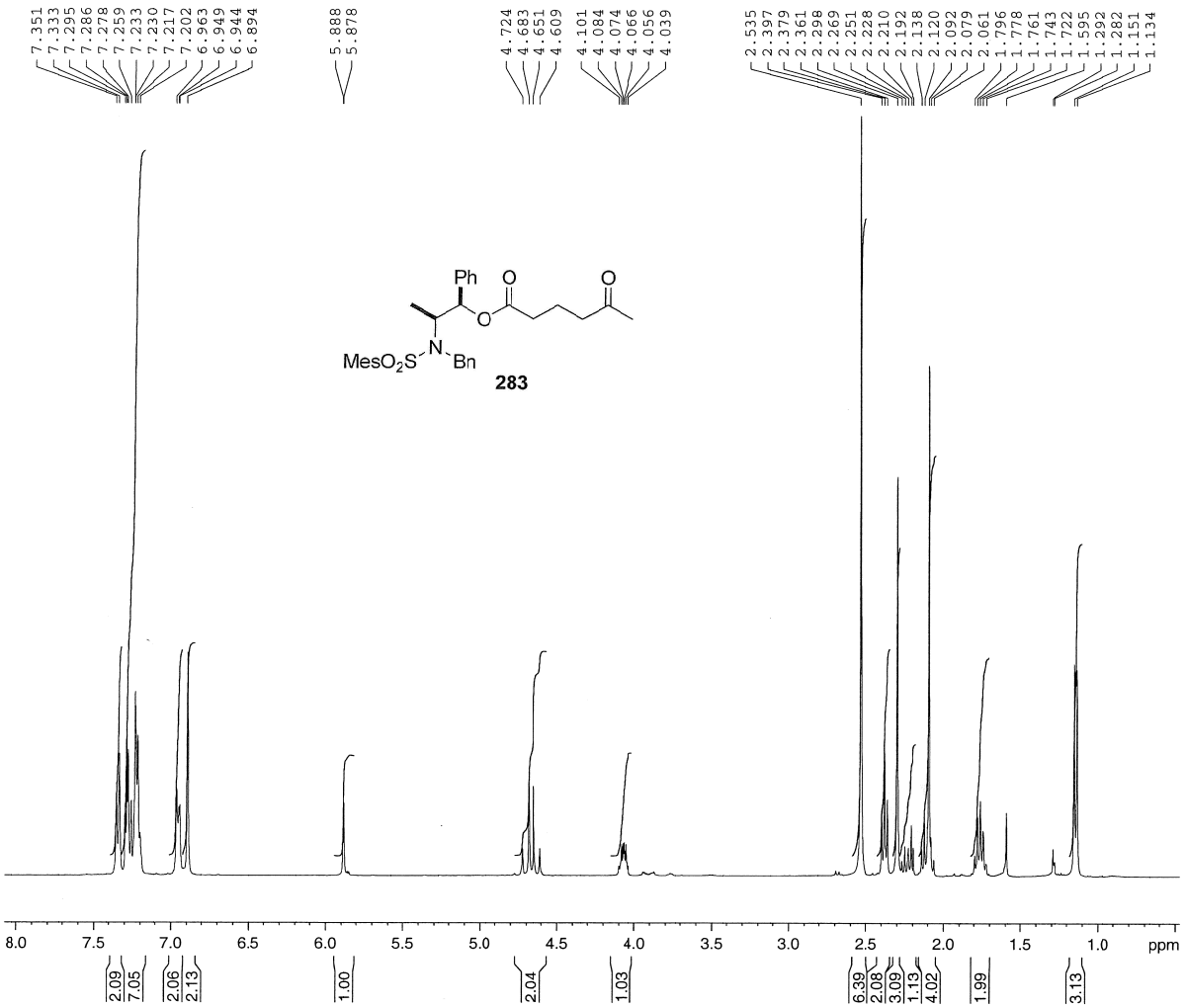

DCC assisted thioester formation (12/5/2008) 15.5 hrs f13-171H NMR_400
Current Data Parameters
NAME ks-T02-19-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20081205
Time 17.58
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
247
7.286
1.685
1.689
1.693
1.700
1.720
1.724
1.734
1.743
1.745
1.750
1.759
1.766
1.769
1.778
1.780
1.782
2.475
2.494
2.508
2.512
3.914
3.931
3.933
3.937
3.942
3.946
3.948
3.957
3.959
3.964
3.968
3.972
3.974
3.992
3.18
9.14
4.24
2.00
3.94
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5


DCC assisted thioester formation (12/5/2008) 15.5 hrs f13-1713C_400
Current Data Parameters
NAME ks-T02-19-1
EXPNO 6
PROCNO 1
DIR /m
USER khomson
F2 - Acquisition Parameters
Date_ 20081205
Time 19.35
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.30421164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
16.60
20.20
23.80
27.54
29.83
31.91
34.15
38.09
44.45
47.80
48.94
60.85
64.67
76.70
77.02
77.34
80.61
101.98
108.67
109.74
115.56
121.20
121.78
126.09
131.52
135.05
144.72
150.38
160.81
173.59
190.25
200.25
205.83
247
ppm

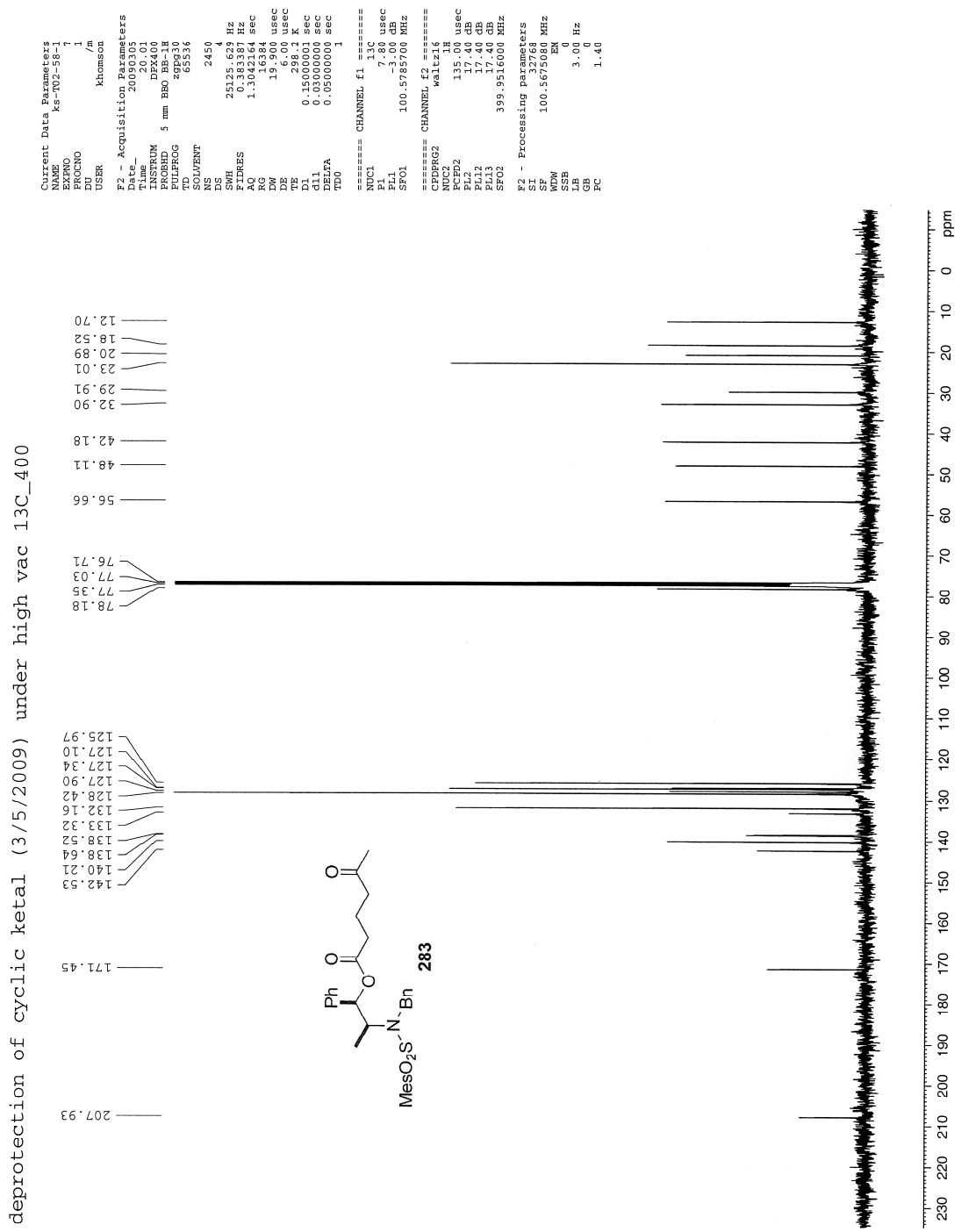

DCC coupling (2/22/2009) f32-43
Current Data Parameters
NAME ks-T02-49-1
EXPNO 8
PROCNO 1
DIR /m
USER khamson
P2 - Acquisition Parameters
Date_ 20090222
Time 16.19
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 203.2
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 199.9528000 MHz
P2 - Processing parameters
SI 32768
SF 199.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.40
Ph
O
O
O
MesO2S
N
Bn
280
ppm

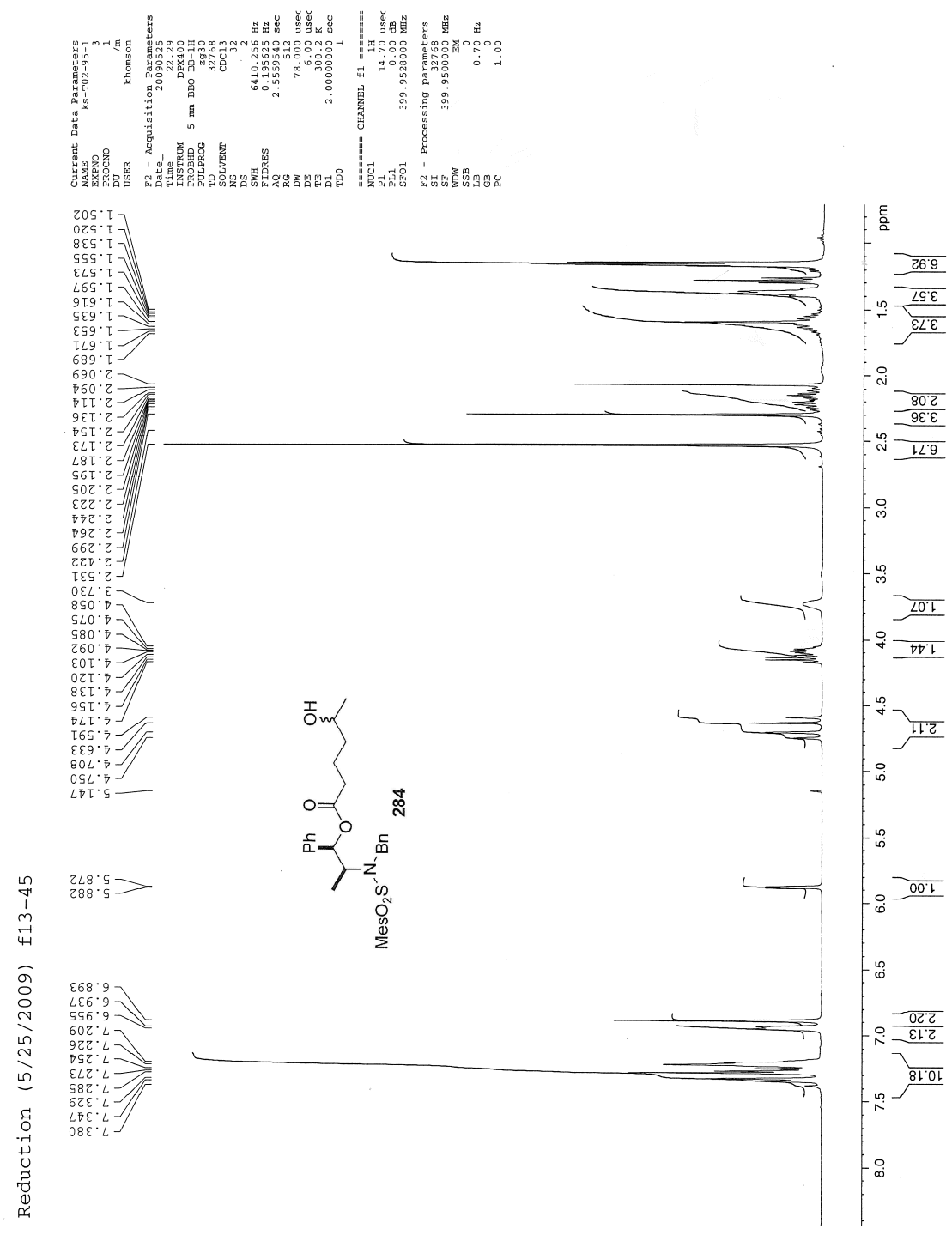

DCC coupling (2/11/2009) f32-43 400_13C
Current Data Parameters
NAME ks-T02-49-1
EXPNO 6
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20090211
Time 16.55
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
12.88
19.22
20.90
23.00
23.75
34.02
38.23
48.17
56.68
64.64
76.72
77.03
77.35
78.03
109.65
125.99
127.11
127.40
127.82
128.37
128.40
132.16
133.36
138.56
138.70
140.23
142.51
171.70
Ph
O
O
O
N
Bn
MesO2S
280
ppm

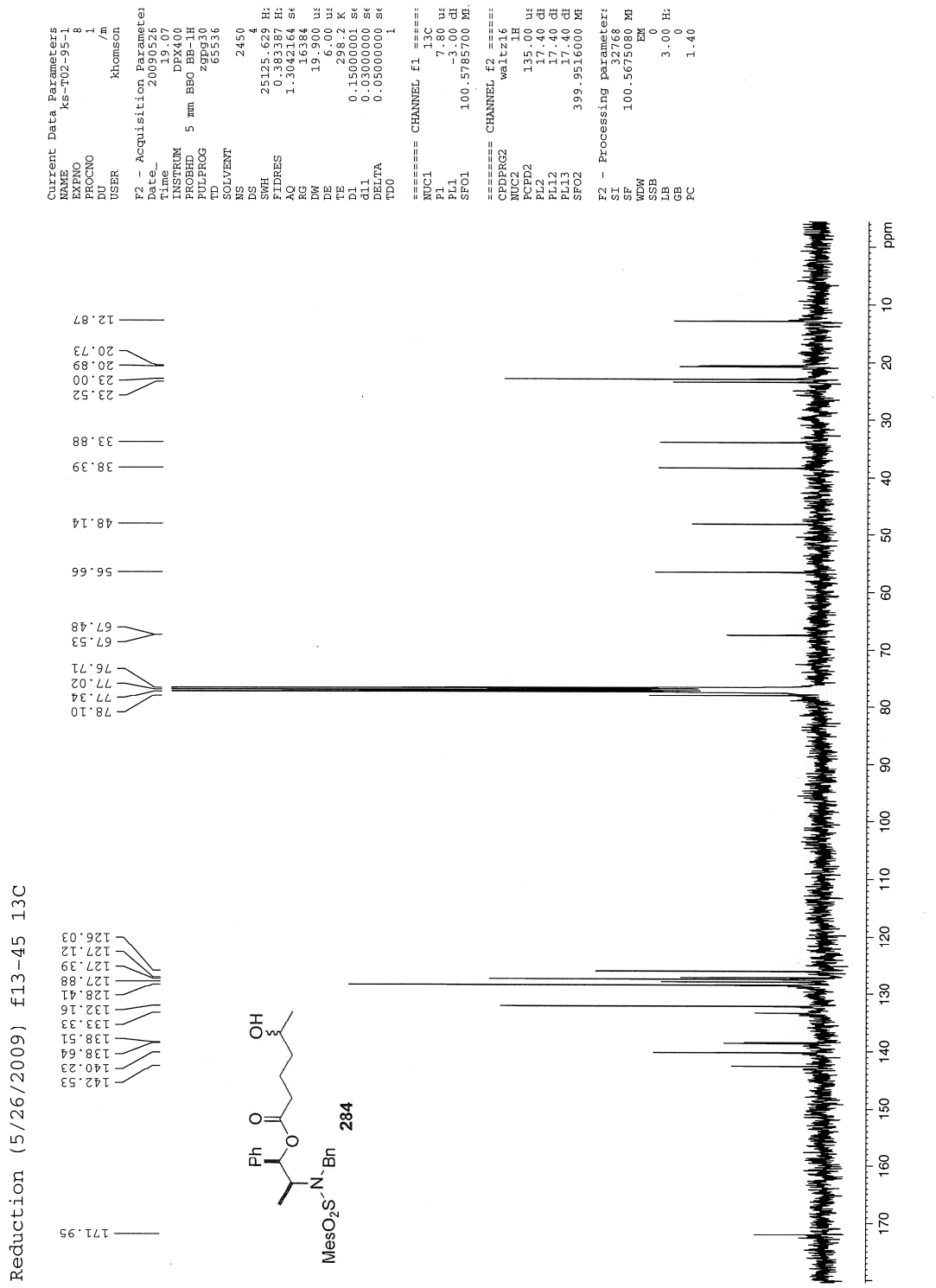
deprotection of cyclic ketal (3/5/2009) under high vac 1H_400

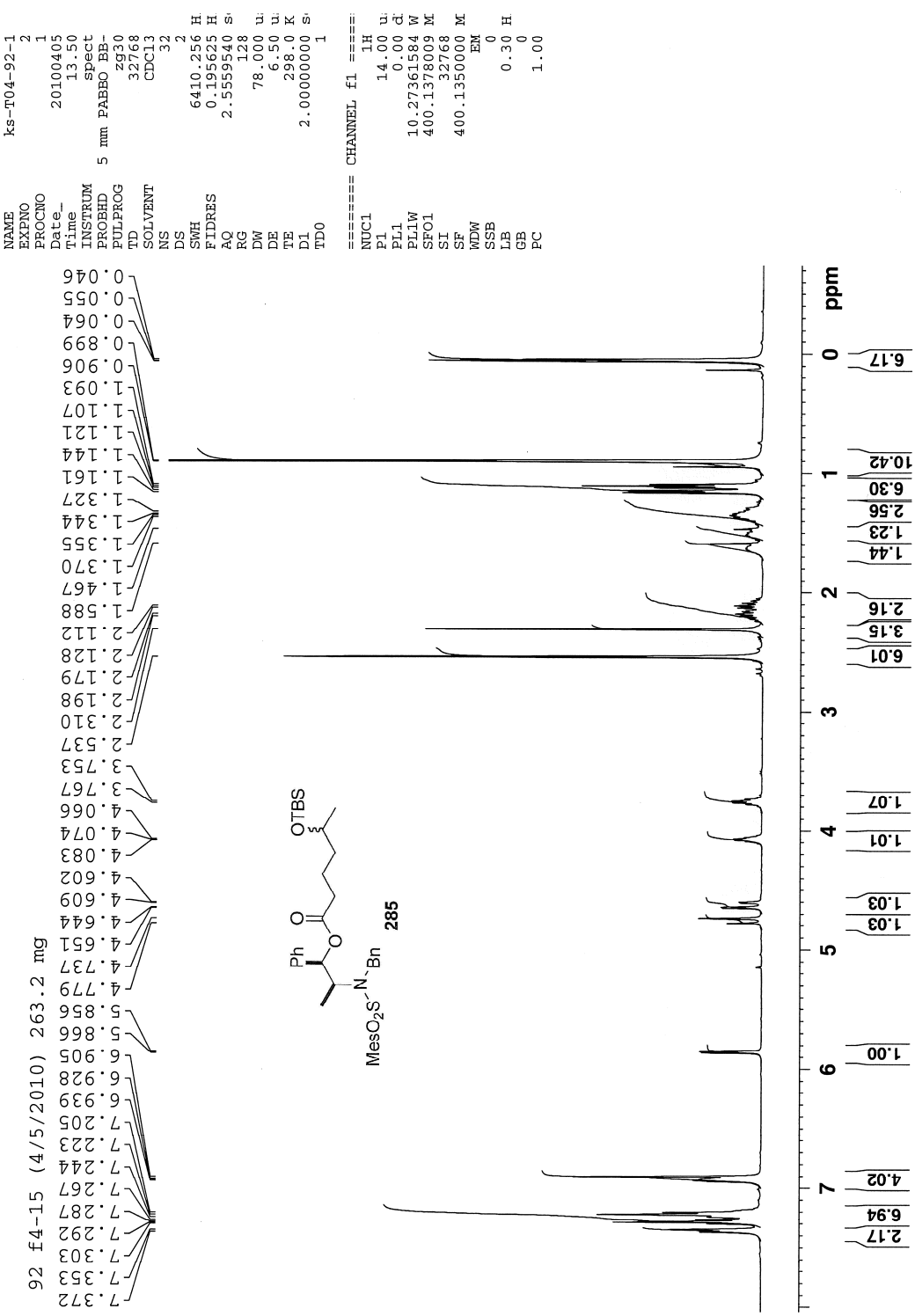


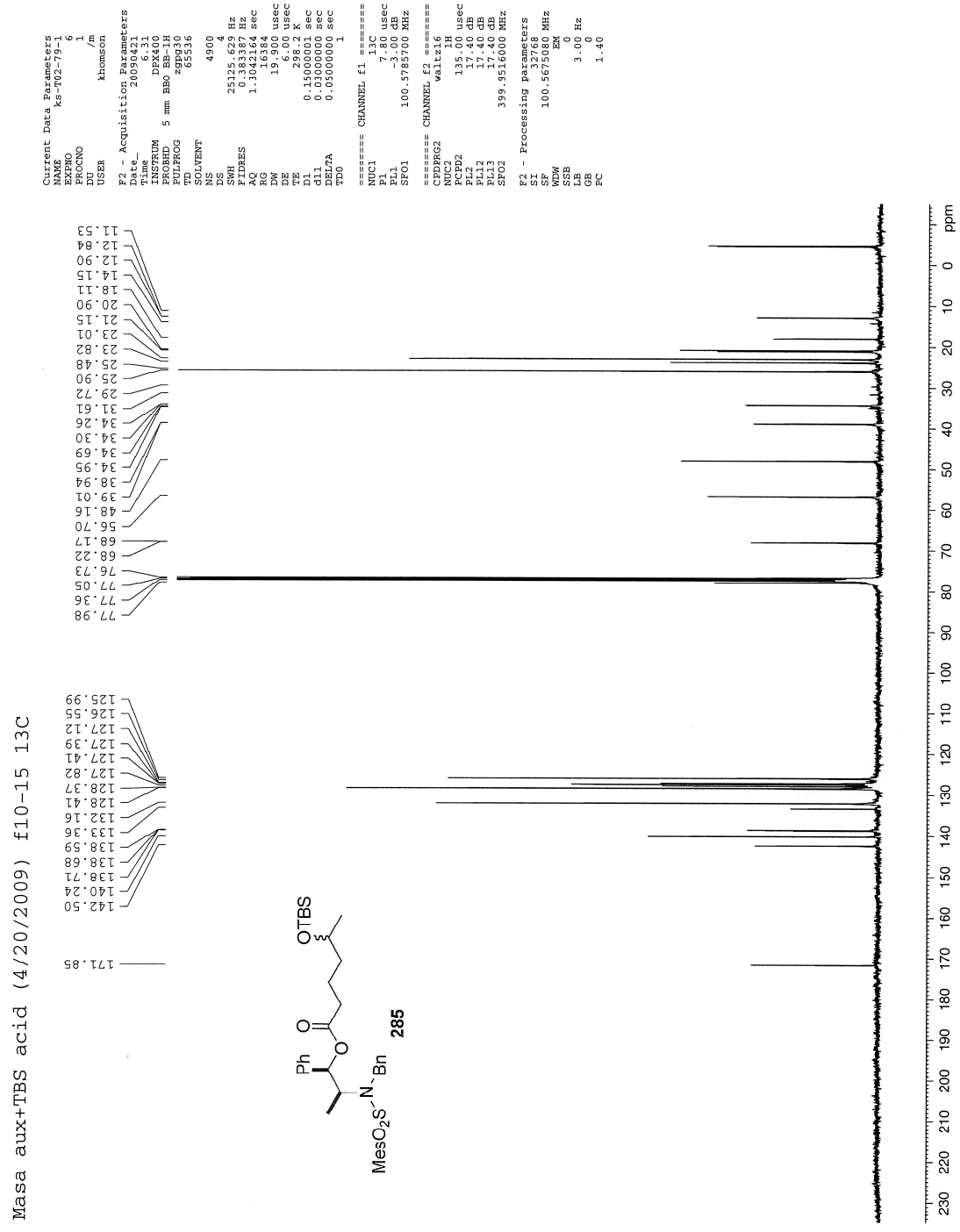

```
Current Data Parameters
NAME          ks-T02-58-1
EXPNO                   3
PROCNO                  1
DU                     /m
USER             khomson

F2 - Acquisition Parameters
Date_           20090305
Time               18.04
INSTRUM          DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 32768
SOLVENT
NS                    32
DS                     2
SWH            6410.256 Hz
FIDRES        0.195625 Hz
AQ            2.5559540 sec
RG                   512
DW                78.000 usec
DE                 6.00 usec
TE                298.2 K
D1           2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                14.70 usec
PL1                0.00 dB
SFO1         399.9528000 MHz

F2 - Processing parameters
SI                 32768
SF           399.9500000 MHz
WDW                   EM
SSB                    0
LB                 0.70 Hz
GB                     0
PC                 1.00
```

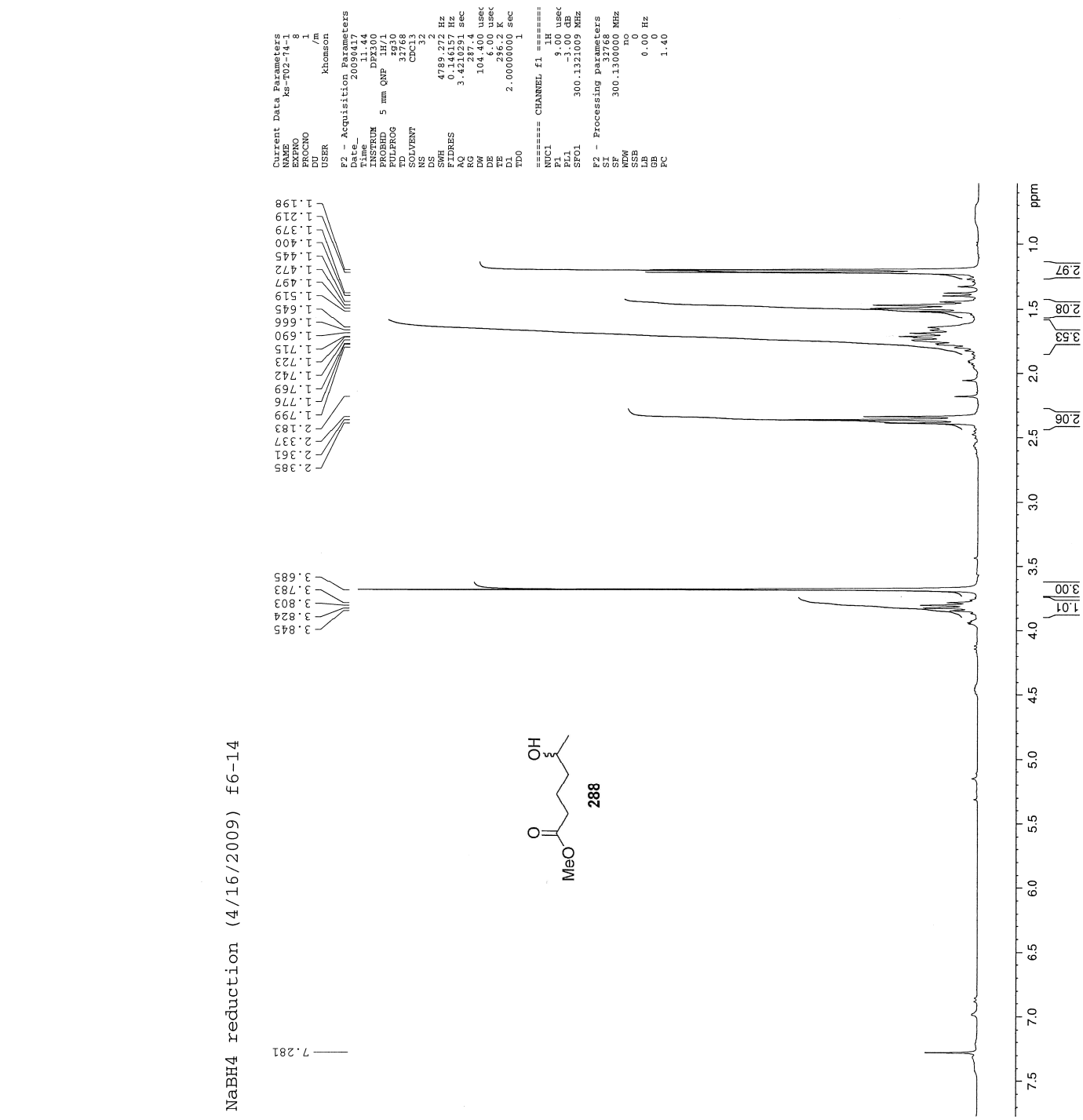

deprotection of cyclic ketal (3/5/2009) under high vac 13C_400
Current Data Parameters
NAME ks-TD2-58-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090305
Time 20.01
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.624 Hz
FIDRES 0.383387 Hz
AQ 1.30442164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
207.93
171.45
142.53
140.21
138.64
138.52
133.32
132.16
128.42
127.90
127.34
127.10
125.97
78.18
77.35
77.03
76.71
56.66
48.11
42.18
32.90
29.91
23.01
20.89
18.52
12.70
Ph
O
O
O
N
Bn
MesO2S
283
ppm

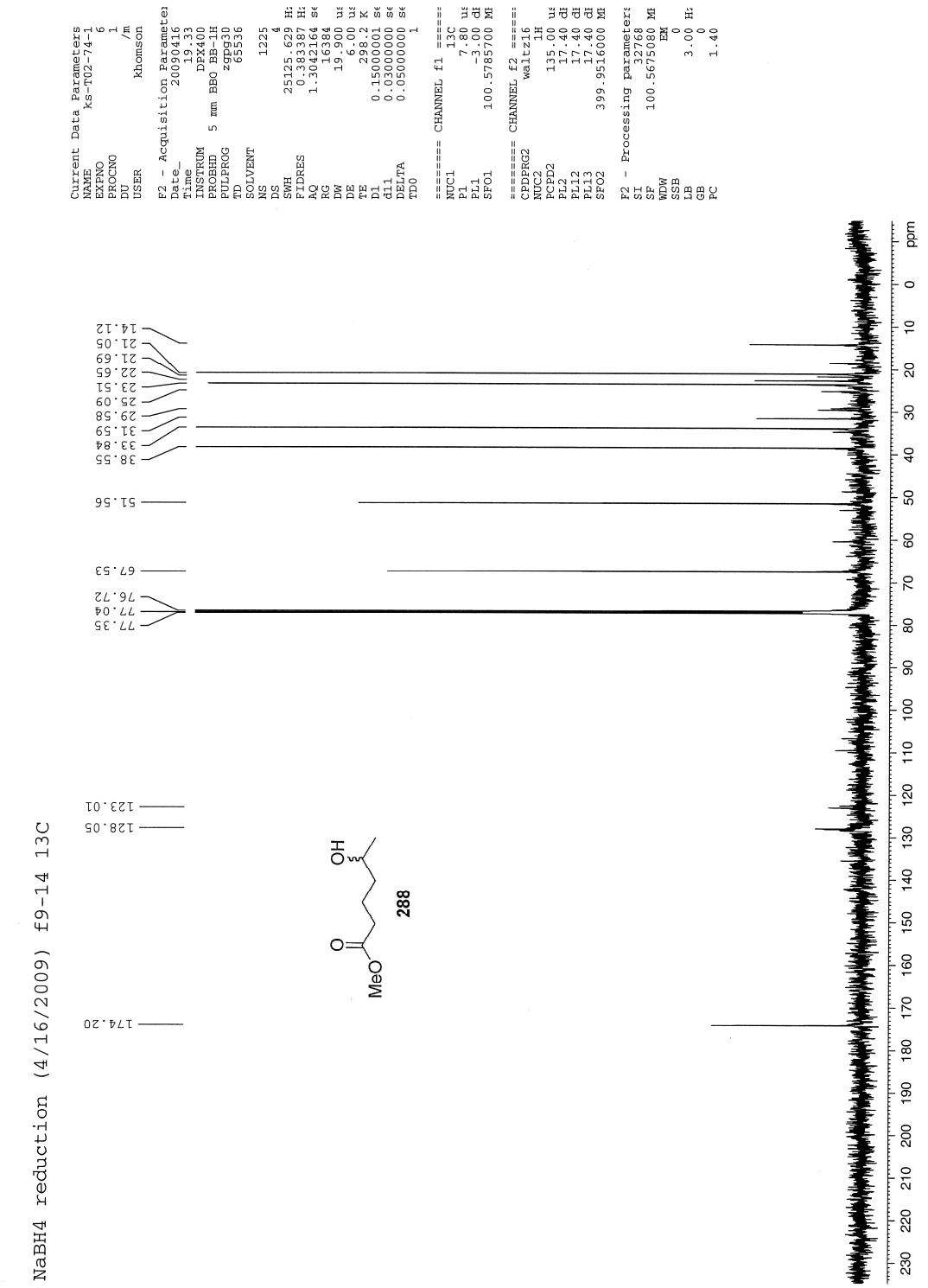

Reduction (5/25/2009) f13-45
Current Data Parameters
NAME ks-702-95-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090525
Time 22:29
INSTRUM DPX400
PROBHD 5 mm BBO BA-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559640 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OH
Ph
O
O
N
Bn
MesO2S
284
ppm

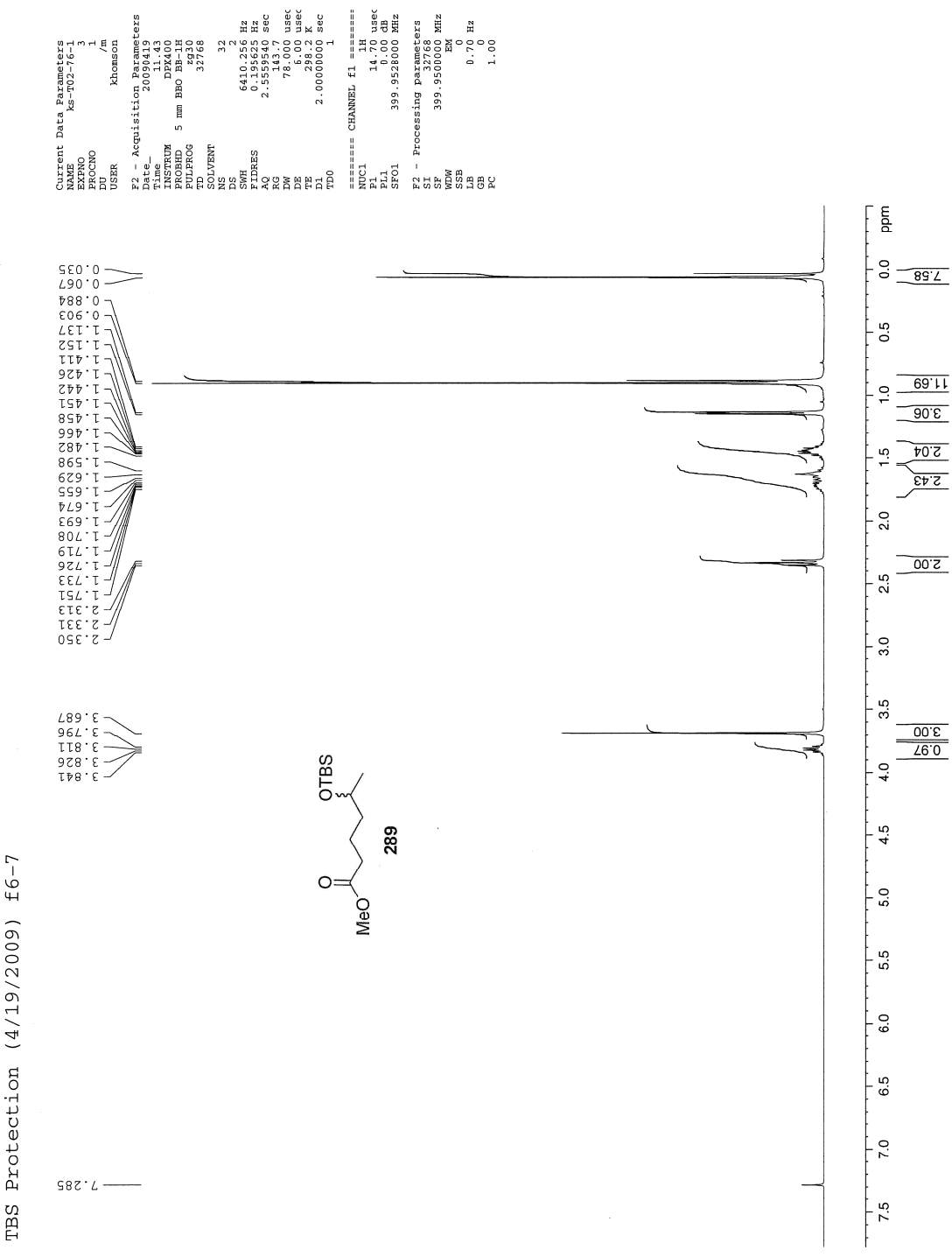

Reduction (5/26/2009) f13-45 13C
Current Data Parameters
NAME ks-TO2-95-1
EXPNO 8
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20090526
Time_ 19.07
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.30421645
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
dl1 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
171.95
142.53
140.23
138.64
138.51
133.33
132.16
128.41
127.88
127.39
127.12
126.03
78.10
77.34
77.02
76.71
67.53
67.48
56.66
48.14
38.39
33.88
23.52
23.00
20.89
20.73
12.87
Ph
O
OH
O
N
Bn
MesO2S
284
ppm


NAME ks-T04-92-1
EXPNO 2
PROCNO 1
Date_ 20100405
Time 13.50
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 128
DW 78.000 u
DE 6.50 u
TE 298.0 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1378009 M
SI 32768
SF 400.1350000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
92 f4-15 (4/5/2010) 263.2 mg
7.372
7.353
7.303
7.292
7.287
7.267
7.244
7.223
7.205
6.939
6.928
6.905
5.866
5.856
4.779
4.737
4.651
4.644
4.609
4.602
4.083
4.074
4.066
3.767
3.753
2.537
2.310
2.198
2.179
2.128
2.112
1.588
1.467
1.370
1.355
1.344
1.327
1.161
1.144
1.121
1.107
1.093
0.906
0.899
0.064
0.055
0.046
OTBS
Ph
O
O
N
Bn
MesO2S
285
ppm
0
1
2
3
4
5
6
7
6.17
10.42
6.30
2.56
1.23
1.44
2.16
3.15
6.01
1.07
1.01
1.03
1.03
1.00
4.02
6.94
2.17


Masa aux+TBS acid (4/20/2009) f10-15 13C
Current Data Parameters
NAME ks-T02-79-1
EXPNO 6
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090421
Time 6.31
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 4900
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
171.85
142.50
140.24
138.71
138.68
138.59
133.36
132.16
128.41
128.37
127.82
127.41
127.39
127.12
126.55
125.99
77.98
77.36
77.05
76.73
68.22
68.17
56.70
48.16
39.01
38.94
34.95
34.69
34.30
34.26
31.61
29.72
25.90
25.48
23.82
23.01
21.15
20.90
18.11
14.15
12.90
12.84
11.53
Ph
O
O
OTBS
MesO2S
N
Bn
285
ppm


NaBH4 reduction (4/16/2009) f6-14
Current Data Parameters
NAME Ks-f02-f4-1
EXPNO 8
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090417
Time 11.44
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.422031 sec
RG 287.4
DW 104.400 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
7.281
3.845
3.824
3.803
3.783
3.685
2.385
2.361
2.337
2.183
1.799
1.776
1.769
1.742
1.723
1.715
1.690
1.666
1.645
1.519
1.497
1.472
1.445
1.400
1.379
1.219
1.198
OH
O
MeO
288
1.01
3.00
2.06
3.53
2.08
2.97
ppm


NaBH4 reduction (4/16/2009) f9-14 13C
Current Data Parameters
NAME ks-T02-74-1
EXPNO 6
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20090416
Time_ 19.13
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 1225
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
174.20
128.05
123.01
77.35
77.04
76.72
67.53
51.56
38.55
33.84
31.59
29.58
25.09
23.51
22.65
21.69
21.05
14.12
OH
O
MeO
288
ppm


TBS Protection (4/19/2009) f6-7
Current Data Parameters
NAME ks-TO2-76-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
P2 - Acquisition Parameters
Date_ 20091419
Time 11.43
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 143.7
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
P2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OTBS
O
MeO
289
7.285
3.841
3.826
3.811
3.796
3.687
2.350
2.331
2.313
1.751
1.733
1.726
1.719
1.708
1.693
1.674
1.655
1.629
1.598
1.482
1.466
1.458
1.451
1.442
1.426
1.411
1.152
1.137
0.903
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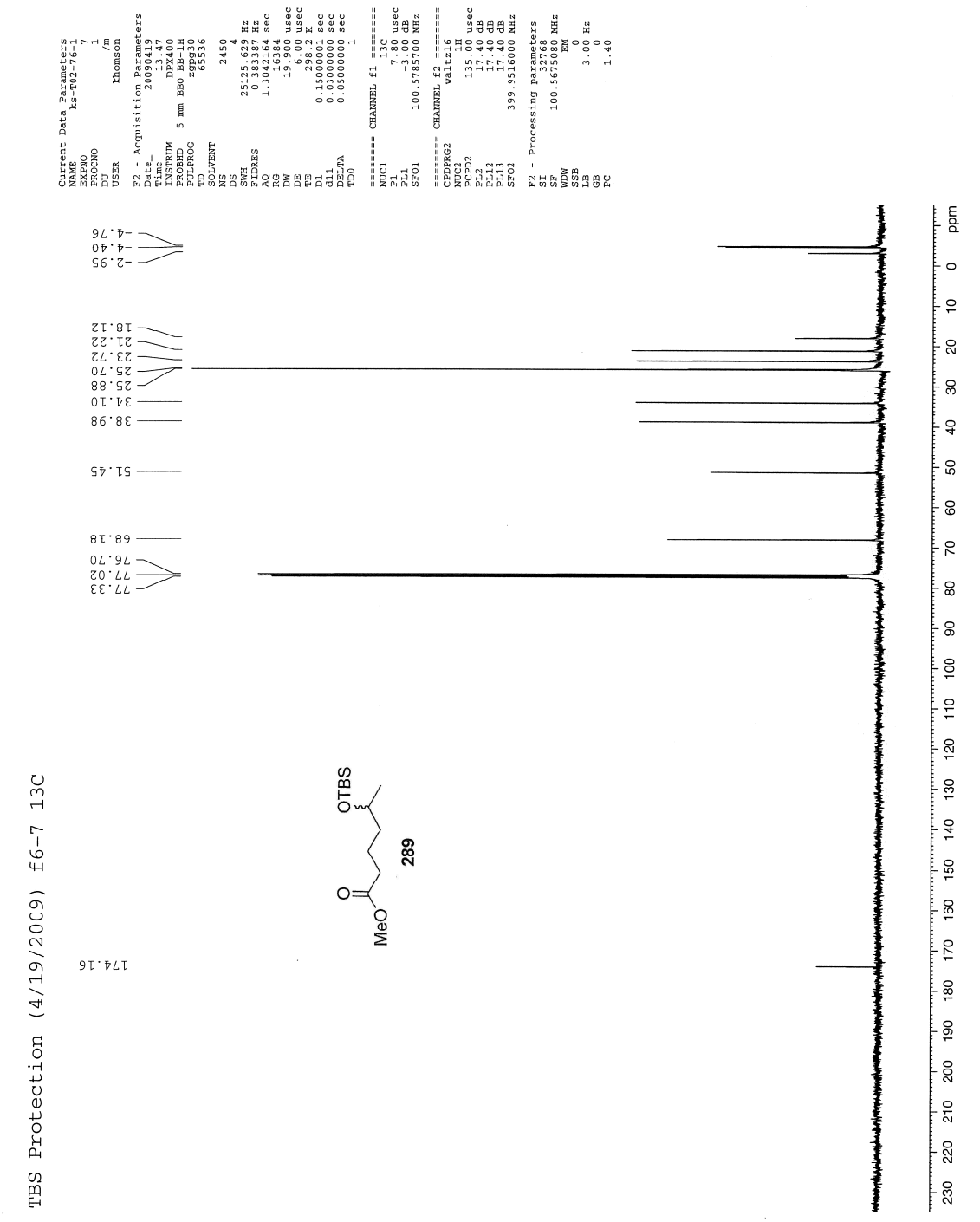
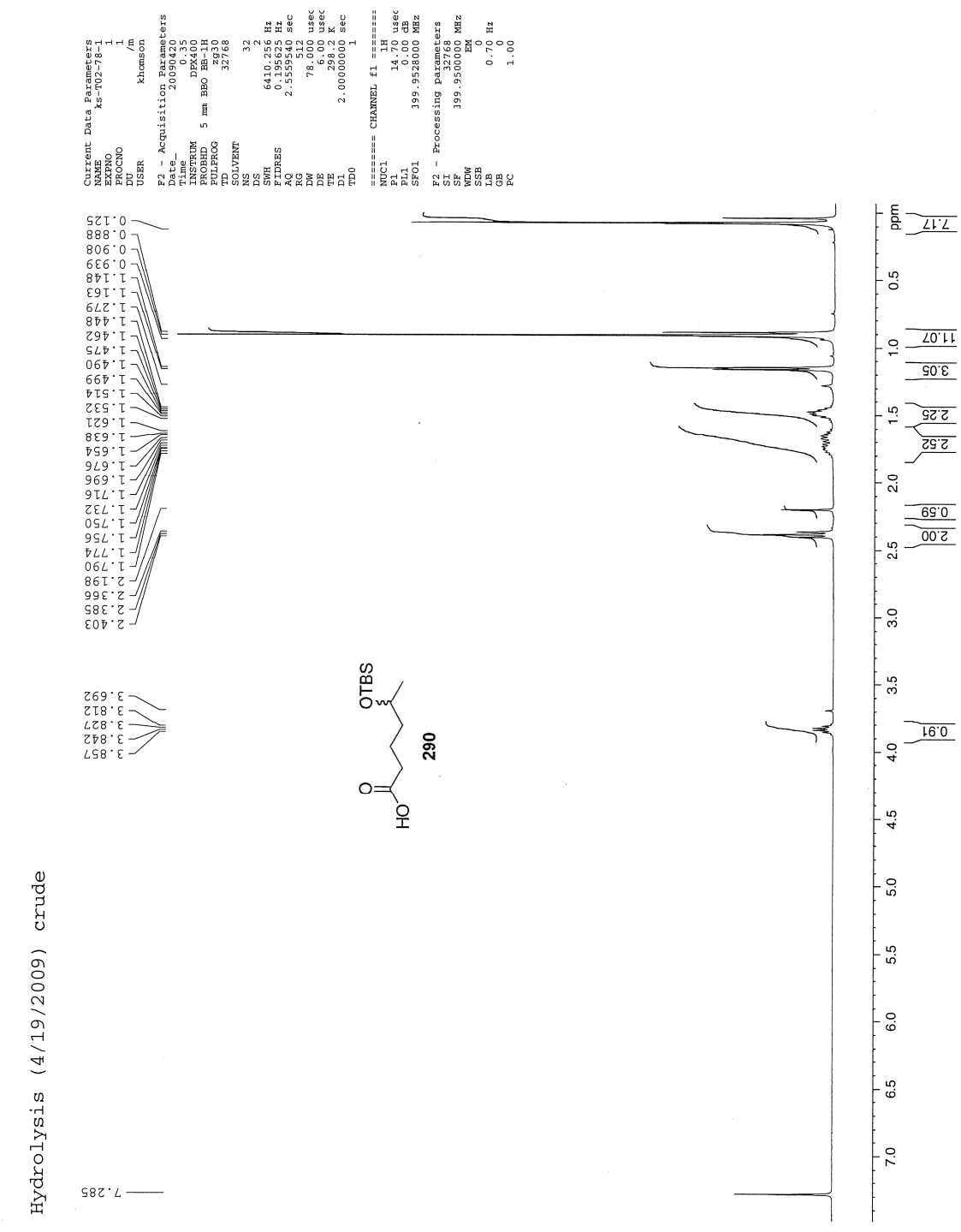
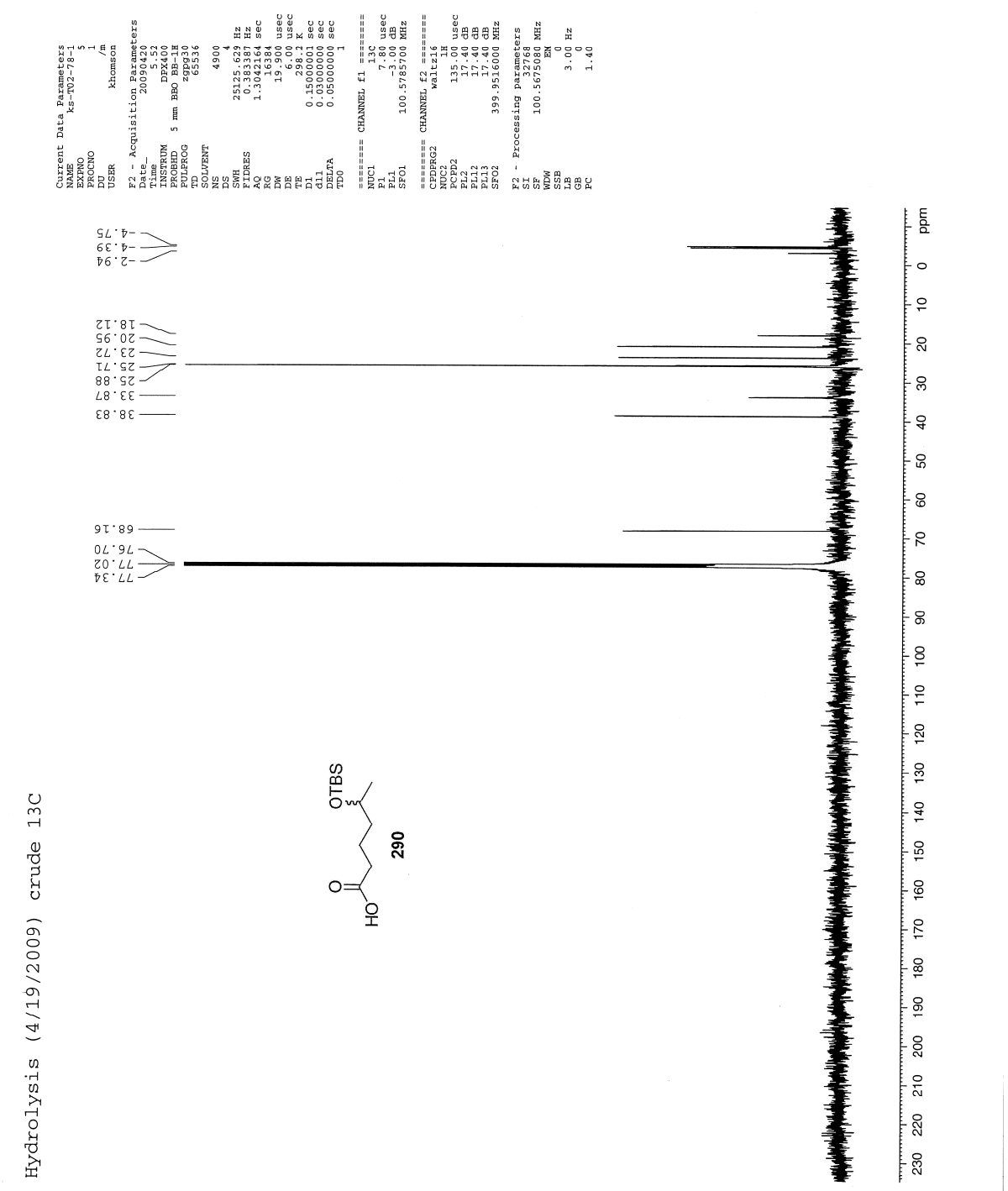
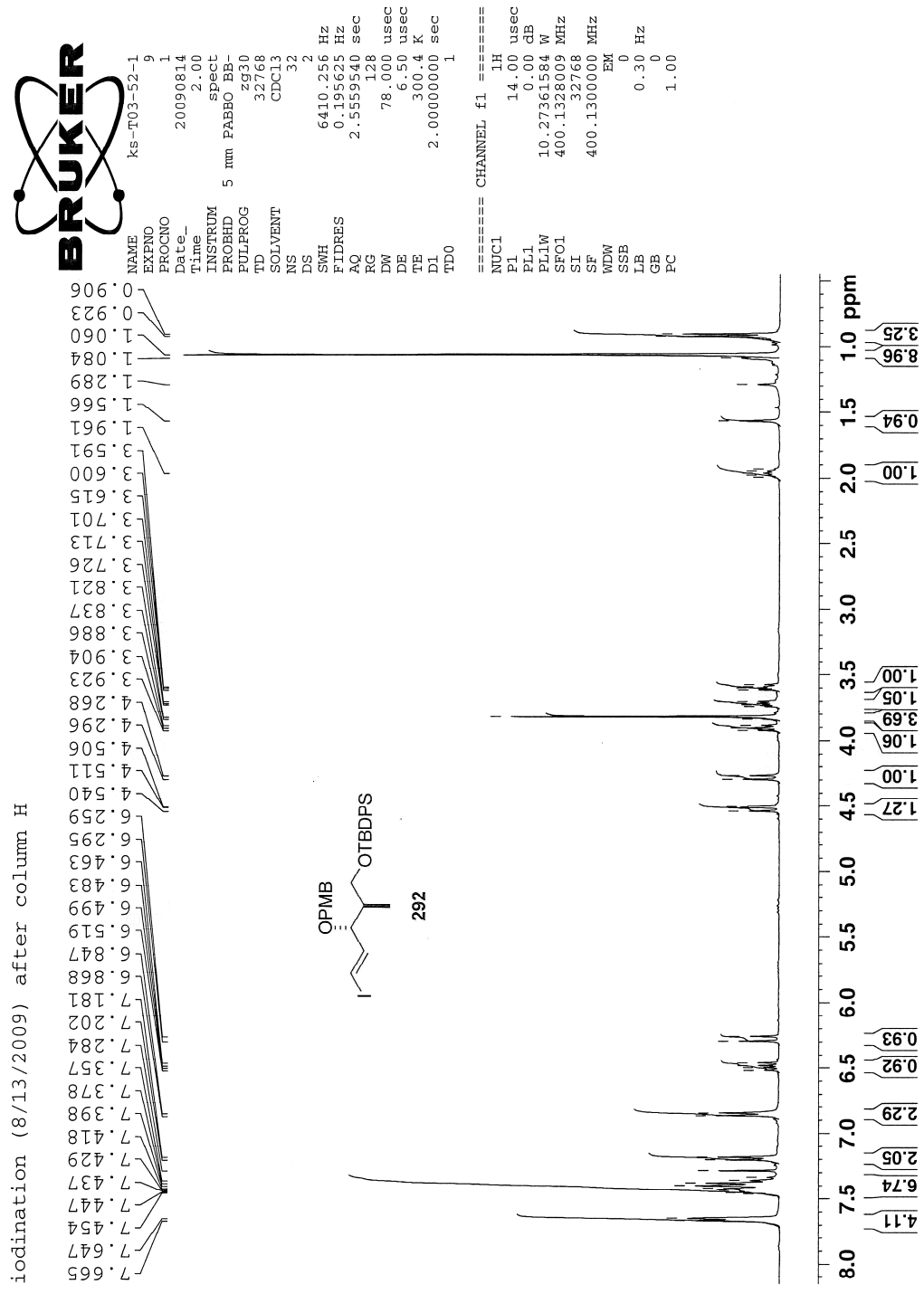
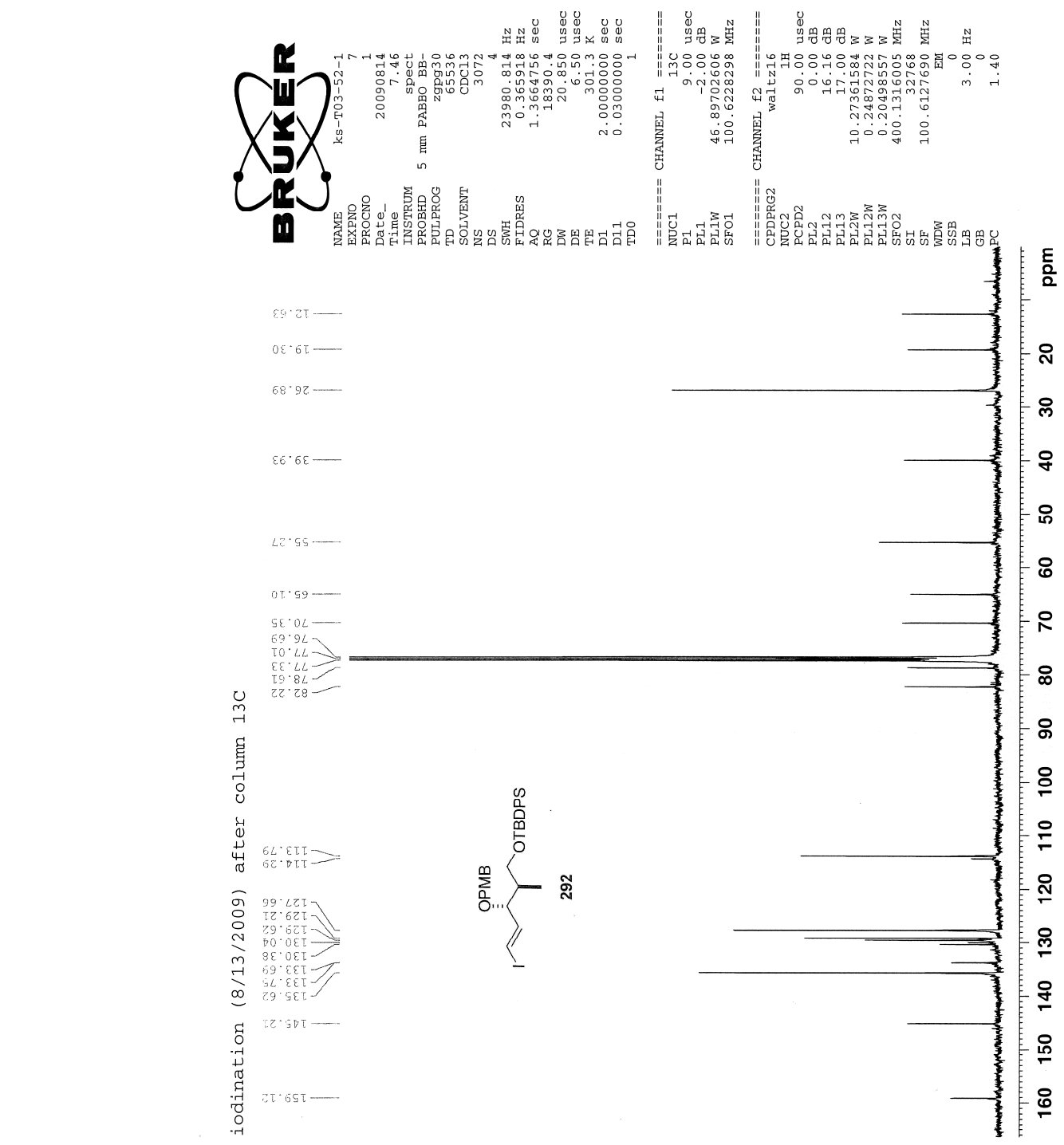
7.58
11.69
3.06
2.04
2.43
2.00
3.00
0.97
ppm

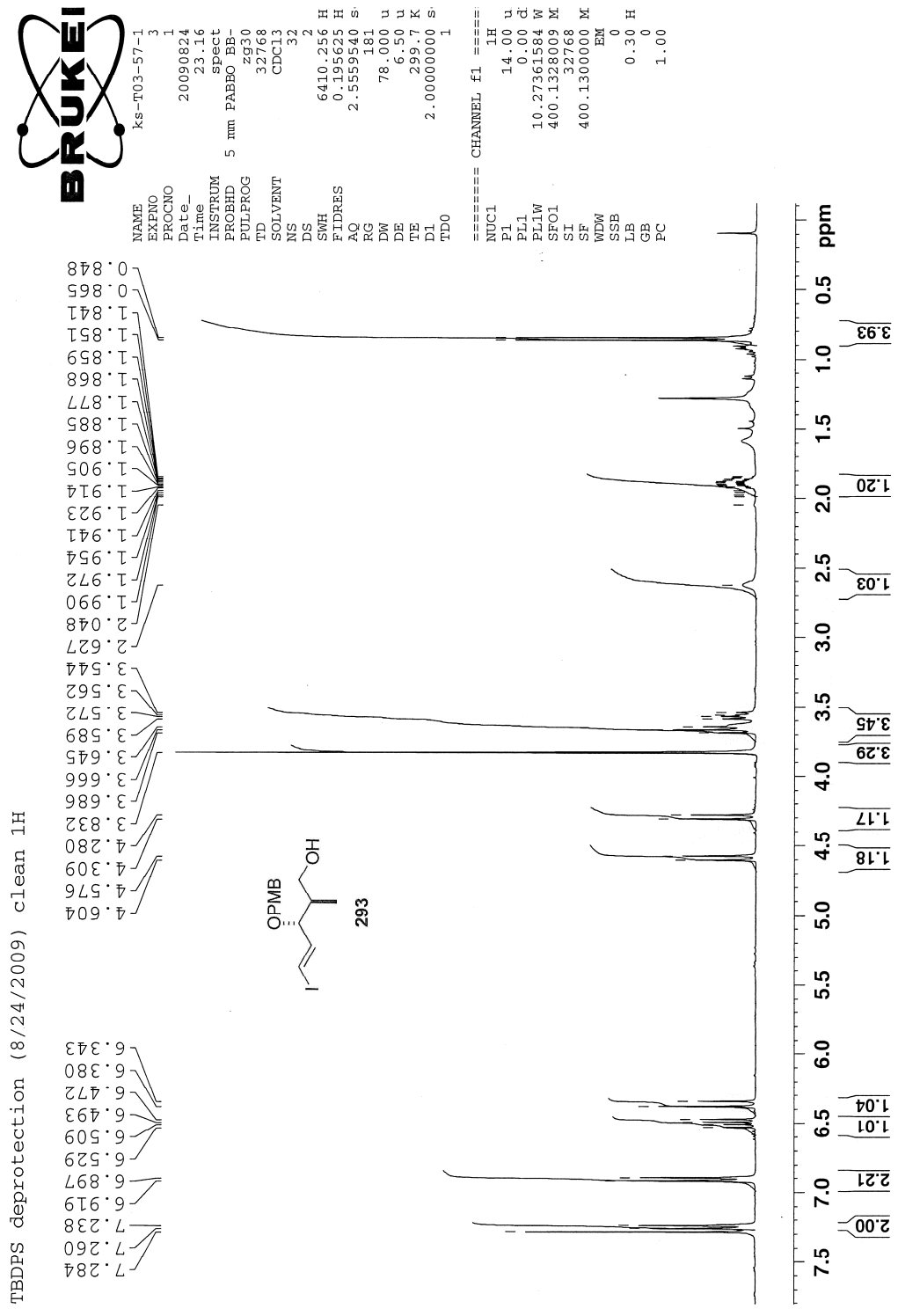

TBS Protection (4/19/2009) f6-7 13C
Current Data Parameters
NAME ks-T02-76-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090419
Time_ 13.47
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000000 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
-4.76
-4.40
-2.95
18.12
21.22
23.72
25.70
25.88
34.10
38.98
51.45
68.18
76.70
77.02
77.33
174.16
OTBS
O
MeO
289
ppm

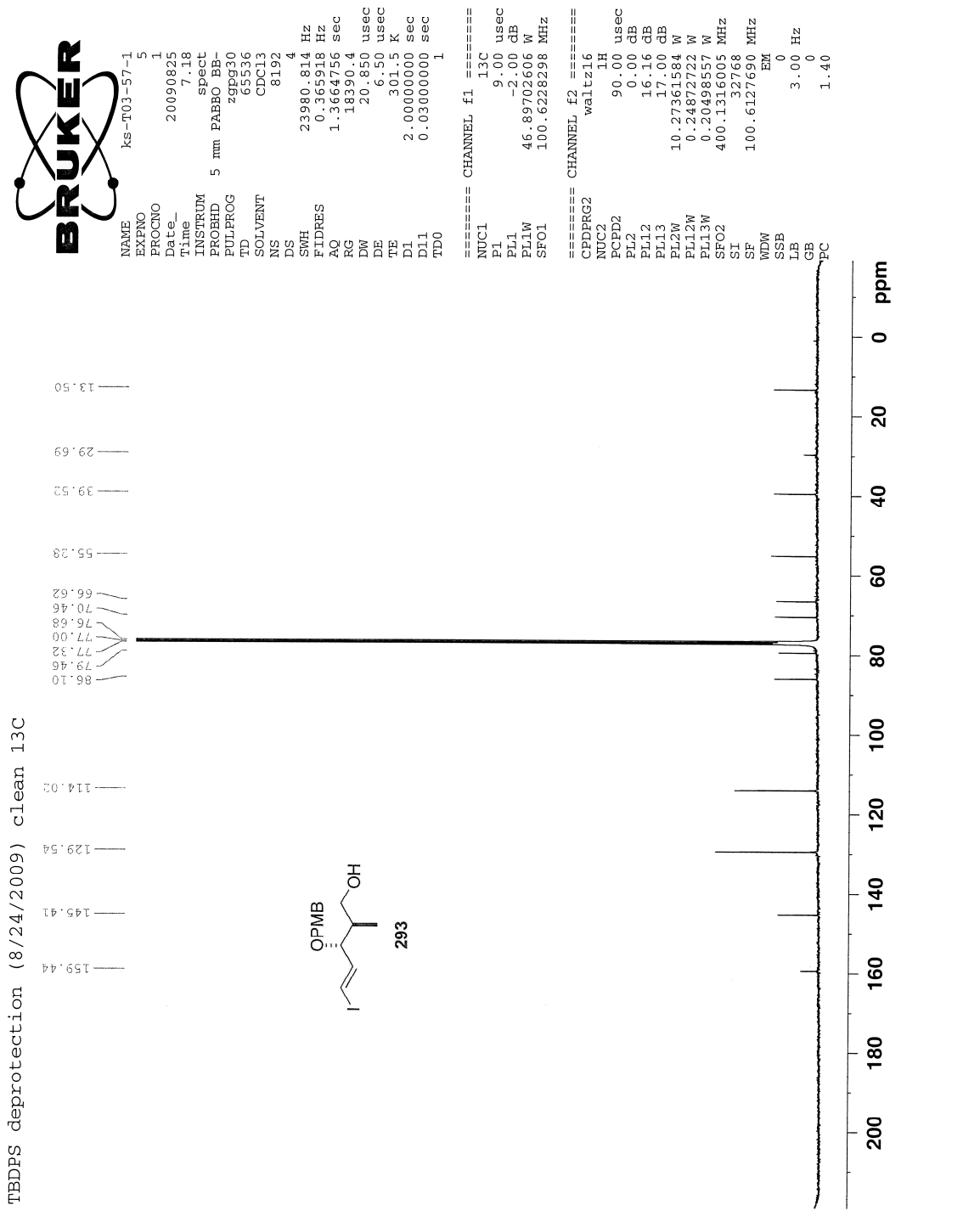

Hydrolysis (4/19/2009) crude
Current Data Parameters
NAME ks-702-78-1
EXPNO 1
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090420
Time 0.35
INSTRM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5539540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 199.9528000 MHz
F2 - Processing parameters
SI 32768
SF 199.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OTBS
O
HO
290
7.285
3.857
3.842
3.827
3.812
3.692
2.403
2.385
2.366
2.198
1.790
1.774
1.756
1.750
1.732
1.716
1.696
1.676
1.654
1.638
1.621
1.532
1.514
1.499
1.490
1.475
1.462
1.448
1.279
1.163
1.148
0.939
0.908
0.888
0.125
7.17
11.07
3.05
2.25
2.52
0.59
2.00
0.91
ppm

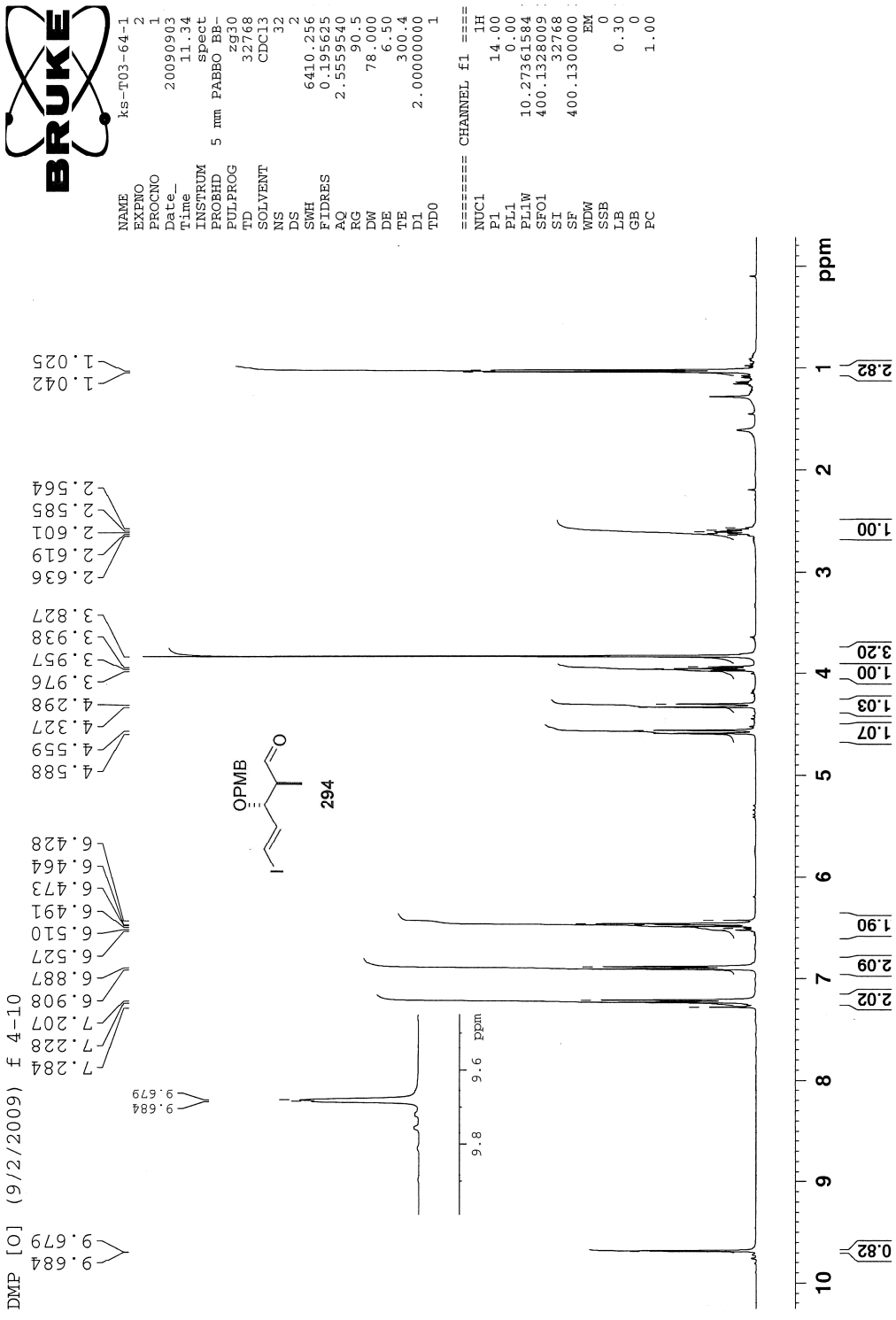

Hydrolysis (4/19/2009) crude 13C
Current Data Parameters
NAME ks-TO2-78-1
EXPNO 5
PROCNO 1
DU /m
USER khomson
P2 - Acquisition Parameters
Date_ 20090420
Time_ 5.52
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 4900
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.30442164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000000 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
77.34
77.02
76.70
68.16
38.83
33.87
25.88
25.71
23.72
20.95
18.12
-2.94
-4.39
-4.75
OTBS
O
HO
290
ppm

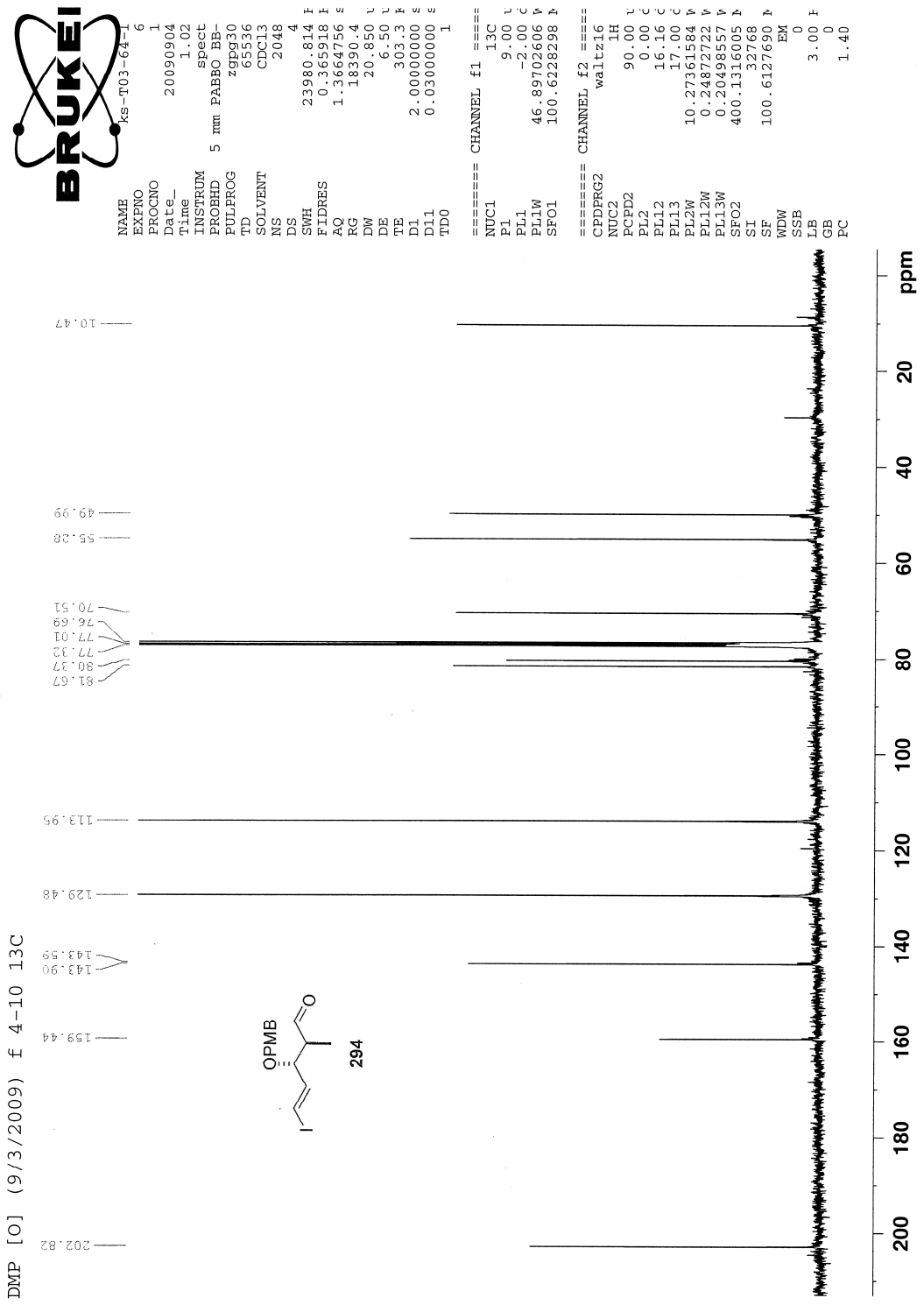

iodination (8/13/2009) after column H
BRUKER
NAME ks-T03-52-1
EXPNO 9
PROCNO 1
Date_ 20090814
Time_ 2.00
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 128
DW 78.000 usec
DE 6.50 usec
TE 300.4 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1328009 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OPMB
OTBDPS
292
ppm

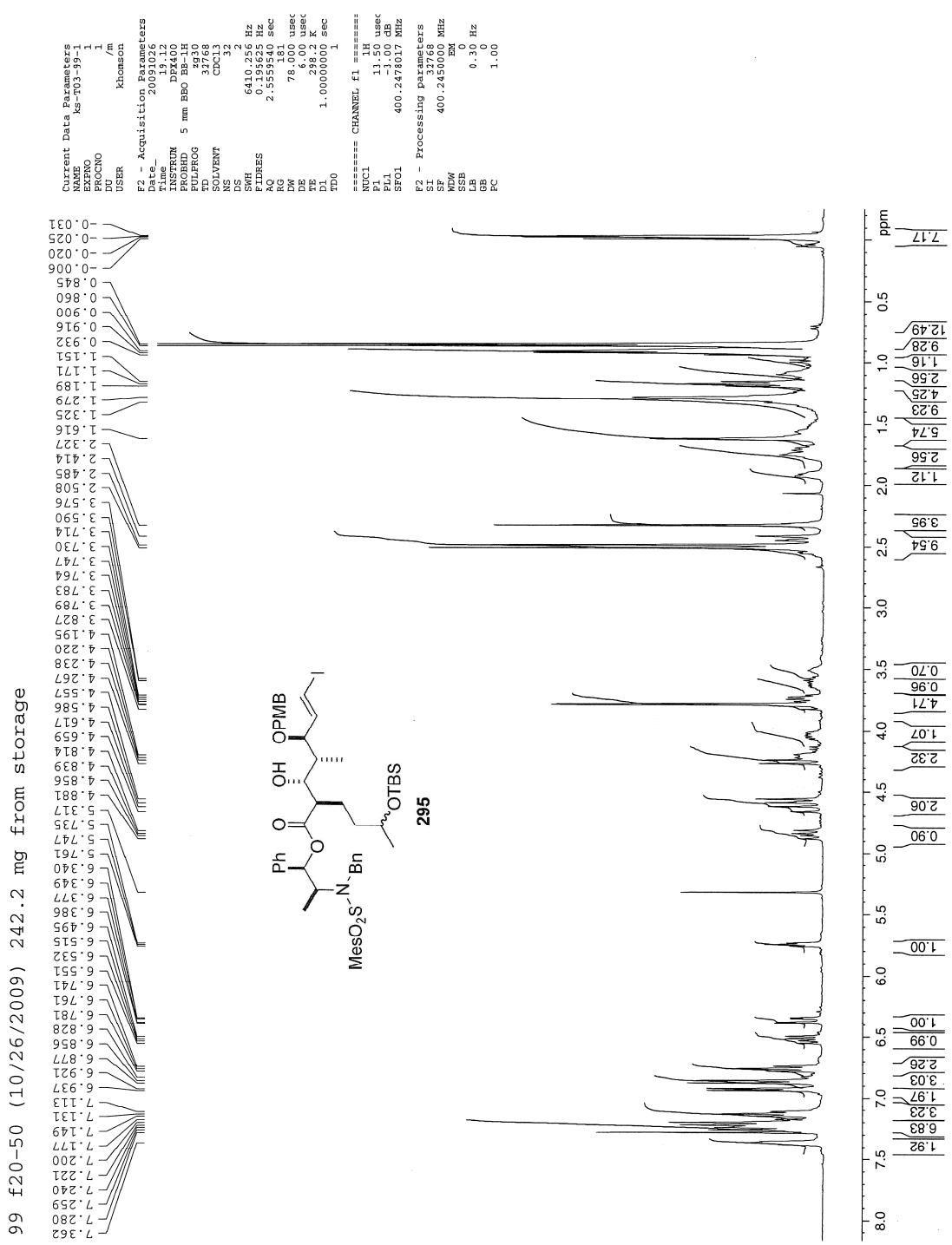

iodination (8/13/2009) after column 13C
OPMB
OTBDPS
I
292
ppm

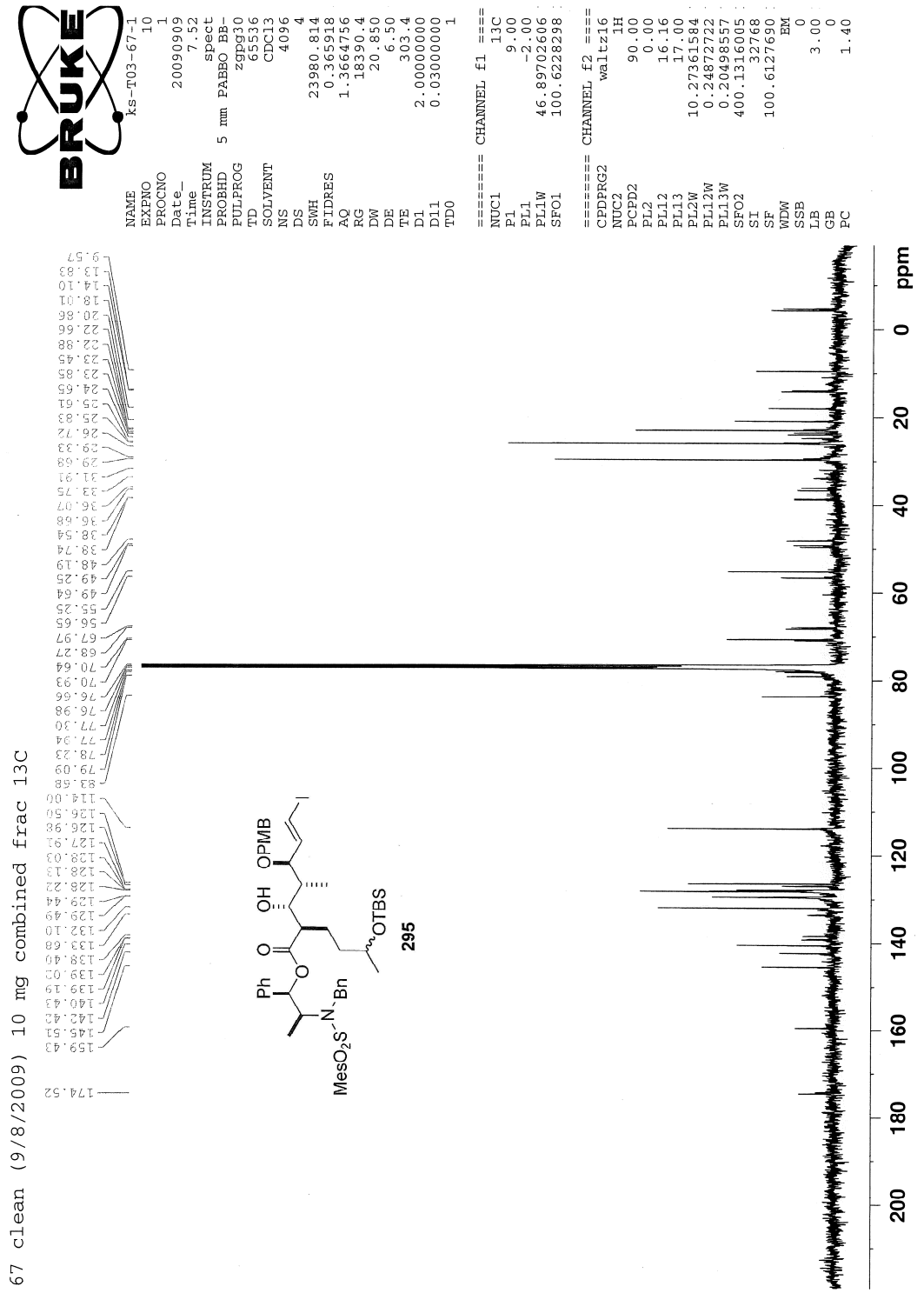

TBDPS deprotection (8/24/2009) clean 1H
ks-T03-57-1
NAME
EXPNO 3
PROCNO 1
Date_ 20090824
Time 23.16
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 181
DW 78.000 u
DE 6.50 u
TE 299.7 K
D1 2.00000000 s
TDO 1
CHANNEL f1
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1328009 M
SI 32768
SF 400.1300000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
OPMB
OH
I
293
ppm
3.93
1.20
1.03
3.45
3.29
1.17
1.18
1.04
1.01
2.21
2.00

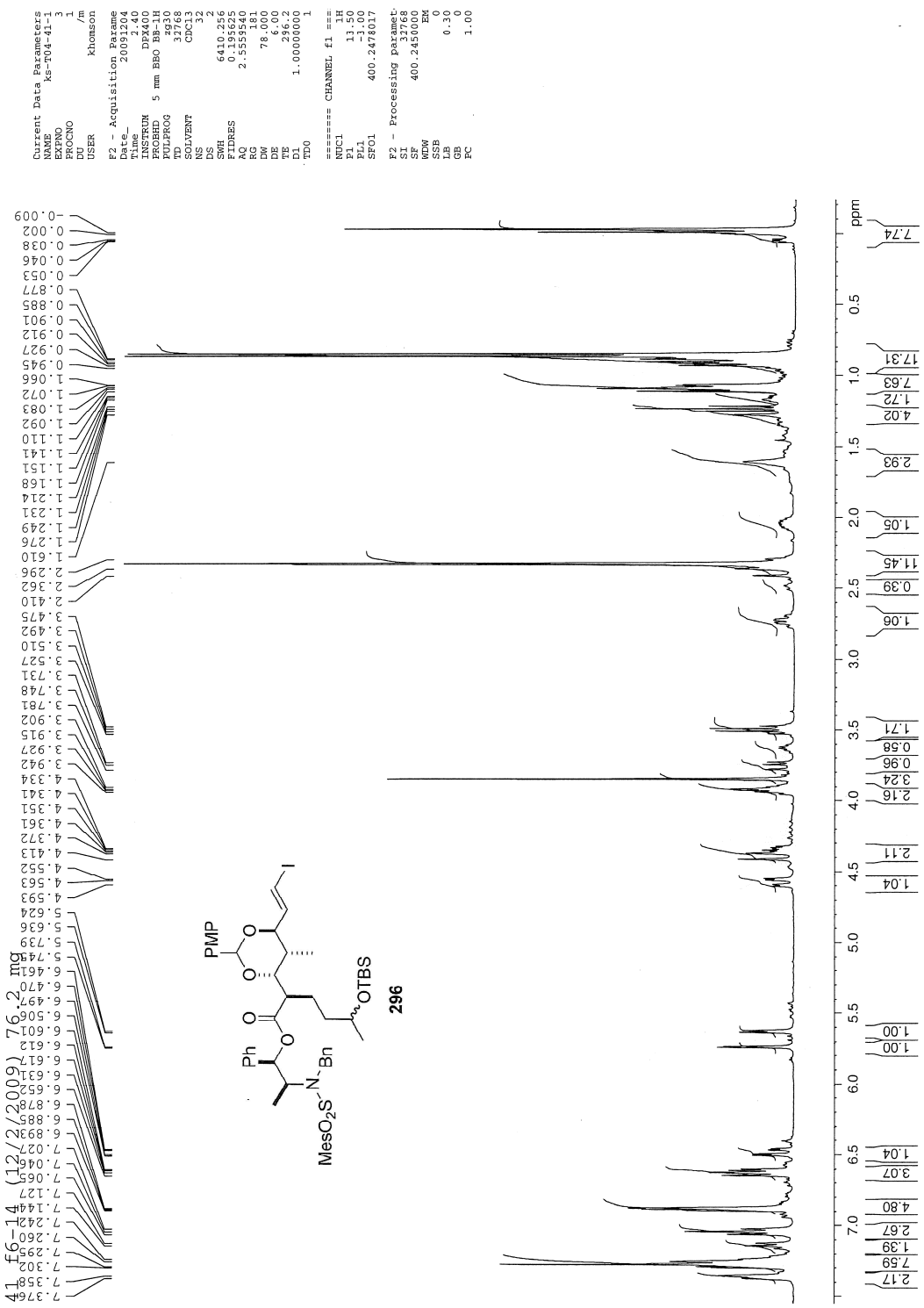

TBDPS deprotection (8/24/2009) clean 13C
NAME ks-T03-57-1
EXPNO 5
PROCNO 1
Date_ 20090825
Time 7.18
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 8192
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 18390.4
DW 20.850 usec
DE 6.50 usec
TE 301.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 -2.00 dB
PL1W 46.89702606 W
SFO1 100.6228298 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 16.16 dB
PL13 17.00 dB
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1316005 MHz
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
13.50
29.69
39.52
55.28
66.62
70.46
76.68
77.00
77.32
79.46
86.10
114.02
129.54
145.41
159.44
OPMB
OH
I
293
200
180
160
140
120
100
80
60
40
20
0
ppm

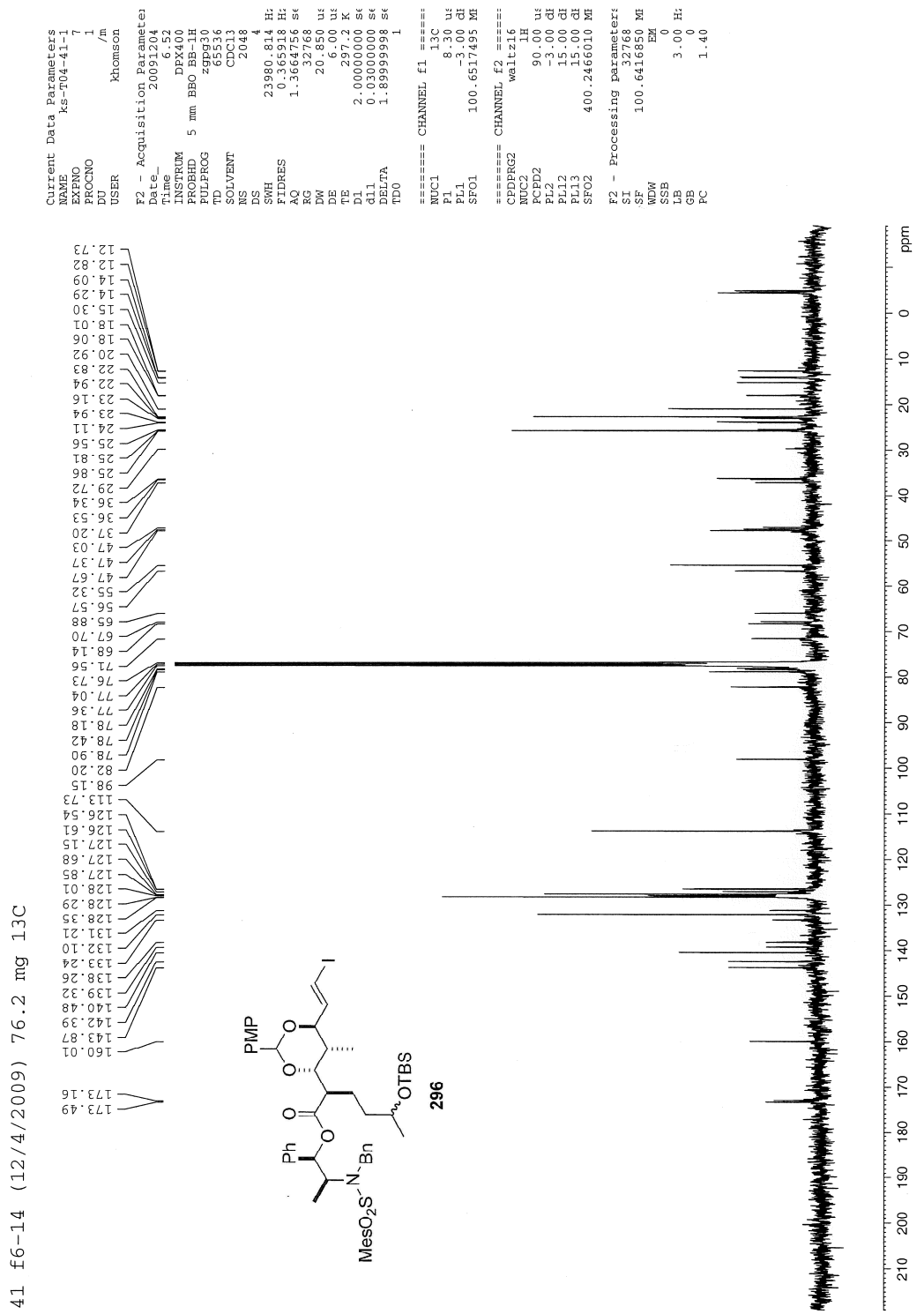

DMP [O] (9/2/2009) f 4-10
ks-T03-64-1
NAME 2
EXPNO 1
PROCNO 20090903
Date_ 11.34
Time spect
INSTRUM 5 mm PABBO BB-
PROBHD zg30
PULPROG 32768
TD CDCl3
SOLVENT 32
NS 2
DS 6410.256
SWH 0.1956625
FIDRES 2.5559540
AQ 90.5
RG 78.000
DW 6.50
DE 300.4
TE 2.00000000
D1 1
TD0
======== CHANNEL f1 ====
NUC1 1H
P1 14.00
PL1 0.00
PL1W 10.27361584
SFO1 400.1328009
SI 32768
SF 400.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
OPMB
294
9.684
9.679
7.284
7.228
7.207
6.908
6.887
6.527
6.510
6.491
6.473
6.464
6.428
4.588
4.559
4.327
4.298
3.976
3.957
3.938
3.827
2.636
2.619
2.601
2.585
2.564
1.042
1.025
ppm
0.82
2.82
1.00
3.20
1.00
1.03
1.07
1.90
2.09
2.02

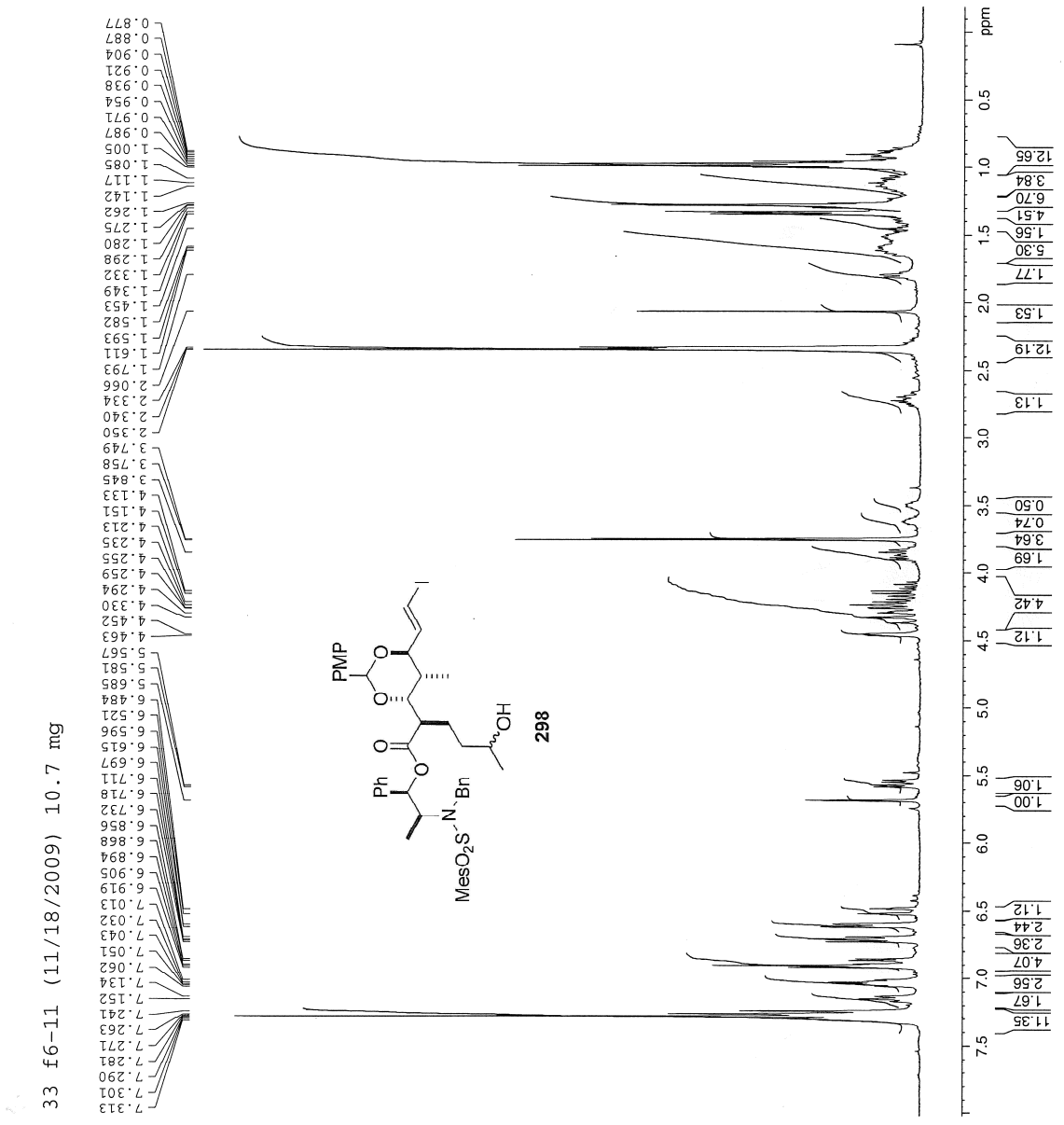

DMP [O] (9/3/2009) f 4-10 13C
ks-T03-64-1
NAME
EXPNO
PROCNO
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
D11
TD0
NUC1
P1
PL1
PL1W
SFO1
CPDPRG2
NUC2
PCPD2
PL2
PL12
PL13
PL2W
PL12W
PL13W
SFO2
SI
SF
WDW
SSB
LB
GB
PC
OPMB
294
202.82
159.44
143.90
143.59
129.48
113.95
81.67
80.37
77.32
77.01
76.69
70.51
55.28
49.99
10.47
ppm

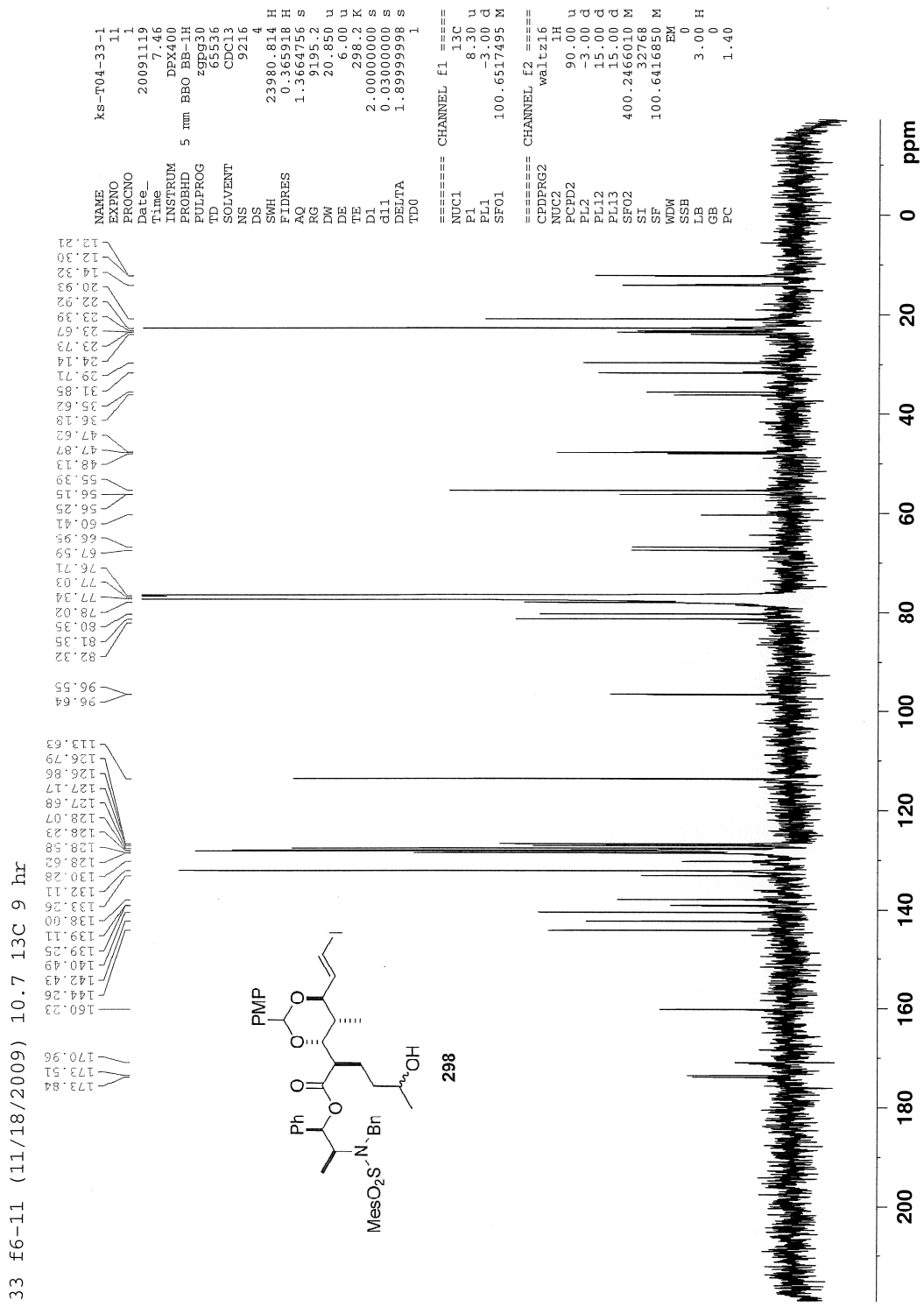

99 f20-50 (10/26/2009) 242.2 mg from storage
Current Data Parameters
NAME ks-T03-99-1
EXPNO 1
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091026
Time 19.13
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Ph
O
OH
OPMB
OTBS
295
MesO2S
N
Bn
ppm

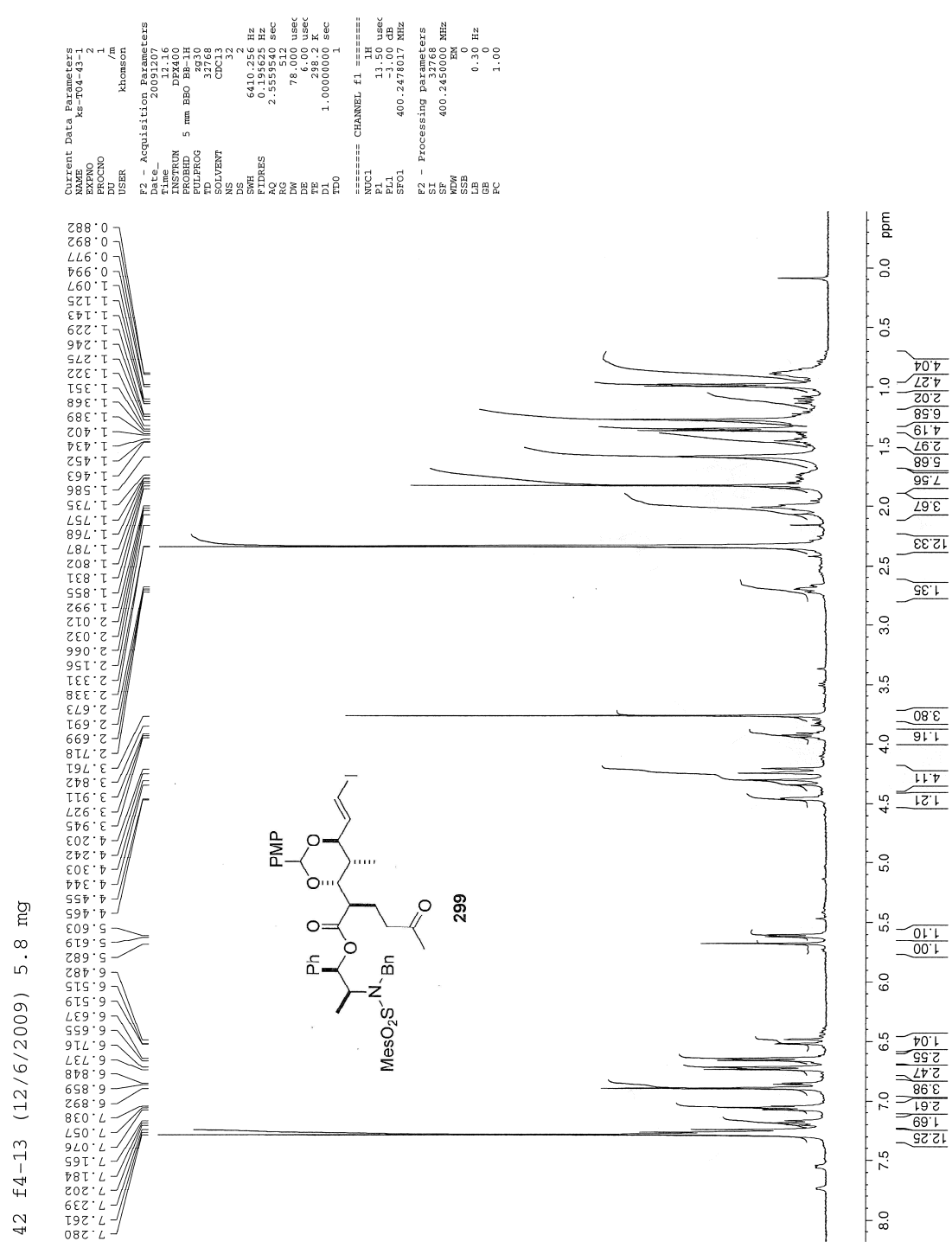

67 clean (9/8/2009) 10 mg combined frac 13C
NAME ks-T03-67-1
EXPNO 10
PROCNO 1
Date_ 20090909
Time_ 7.52
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4096
DS 4
SWH 23980.814
FIDRES 0.365918
AQ 1.3664756
RG 18390.4
DW 20.850
DE 6.50
TE 303.4
D1 2.00000000
D11 0.03000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 9.00
PL1 -2.00
PL1W 46.89702606
SFO1 100.6228298
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00
PL2 0.00
PL12 16.16
PL13 17.00
PL2W 10.27361584
PL12W 0.24872722
PL13W 0.20498557
SFO2 400.1316005
SI 32768
SF 100.6127690
WDW EM
SSB 0
LB 3.00
GB 0
PC 1.40
Ph
O
OH
OPMB
OTBS
MesO2S
N
Bn
295
ppm

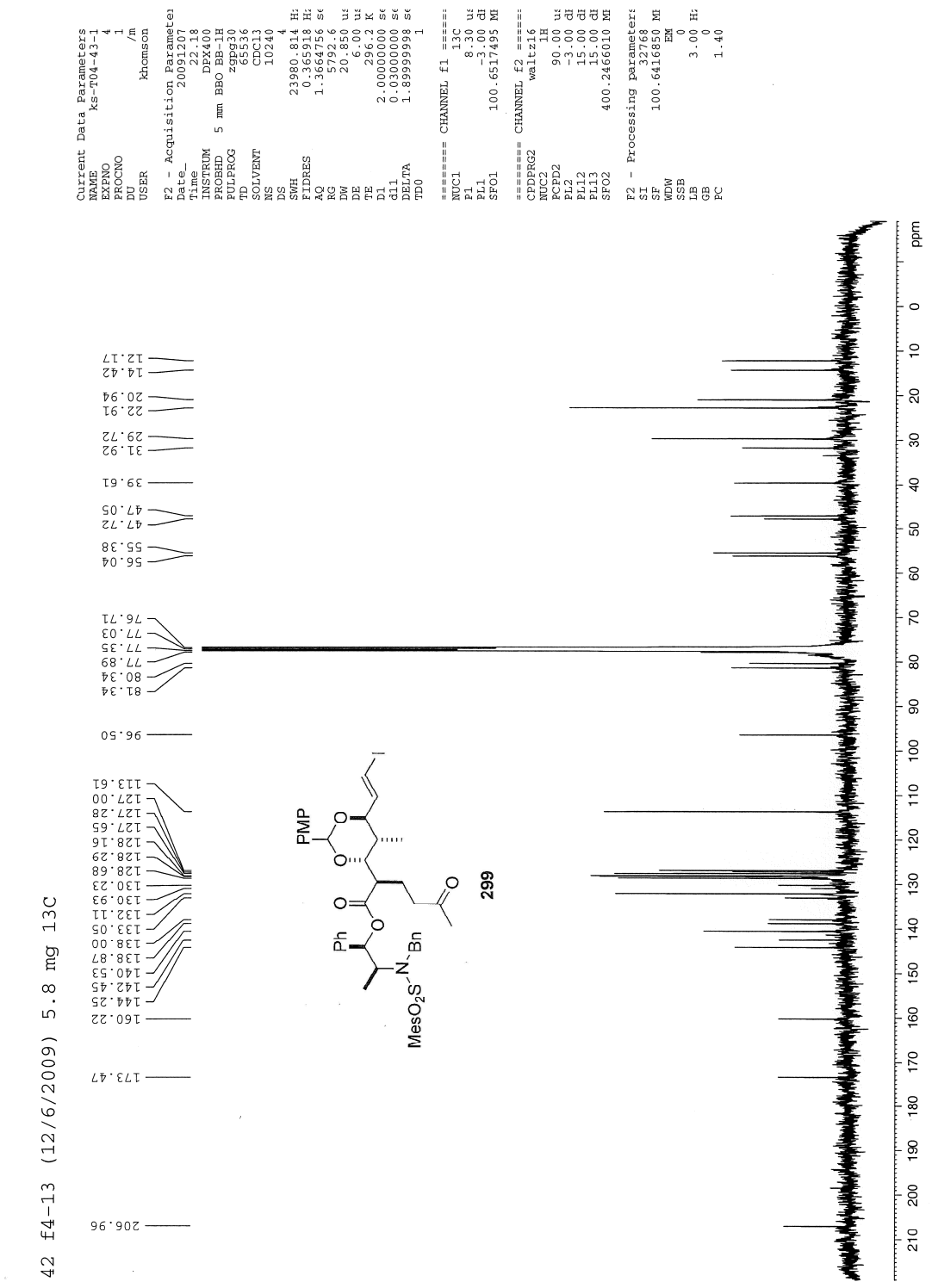

Current Data Parameters
NAME ks-T04-41-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parame
Date_ 20091204
Time 1.40
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 181
DW 78.000
DE 6.00
TE 296.2
D1 1.0000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 11.50
PL1 -1.00
SFO1 400.2478017
F2 - Processing paramet
SI 32768
SF 400.2450000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
41 f6-14 (12/2/2009) 76.2 mg
PMP
Ph
MesO2S
N
Bn
OTBS
296
ppm

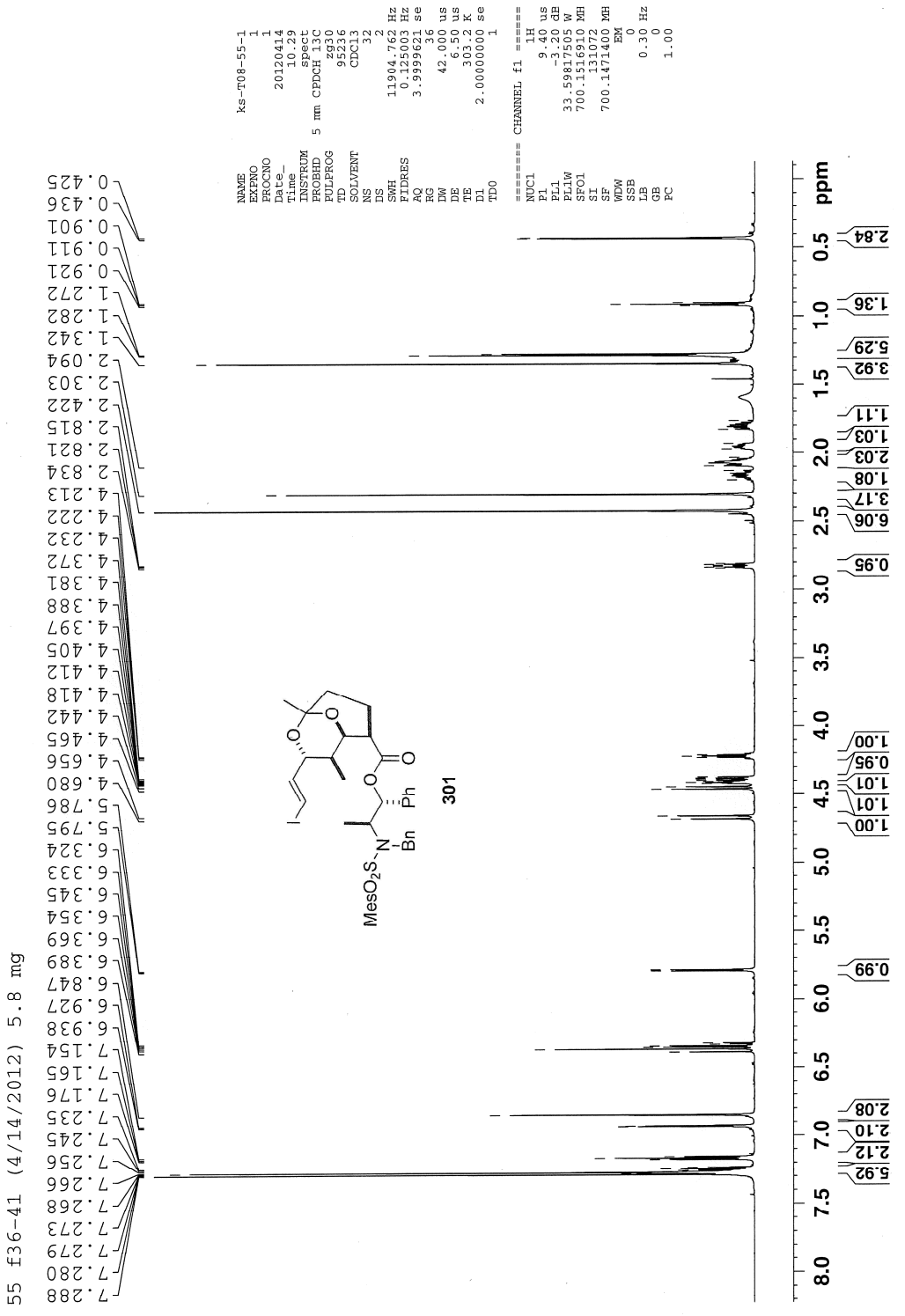

41 f6-14 (12/4/2009) 76.2 mg 13C
Current Data Parameters
NAME ks-T04-41-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20091204
Time_ 6.52
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2048
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 32768
DW 20.850 u
DE 6.00 u
TE 297.2 K
D1 2.00000000 s
d11 0.03000000 s
DELTA 1.89999998 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 8.30 u
PL1 -3.00 d
SFO1 100.6517495 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 -3.00 d
PL12 15.00 d
PL13 15.00 d
SFO2 400.2466010 M
F2 - Processing parameter
SI 32768
SF 100.6416850 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
173.49
173.16
160.01
143.87
142.39
140.48
139.32
138.26
133.24
132.10
131.21
128.35
128.29
128.01
127.85
127.68
127.15
126.61
126.54
113.73
98.15
82.20
78.90
78.42
78.18
77.36
77.04
76.73
71.56
68.14
67.70
65.88
56.57
55.32
47.67
47.37
47.03
37.20
36.53
36.34
29.72
25.86
25.81
25.56
24.11
23.94
23.16
22.94
22.83
20.92
18.06
18.01
15.30
14.29
14.09
12.82
12.73
PMP
Ph
MesO2S
N
Bn
OTBS
296
ppm

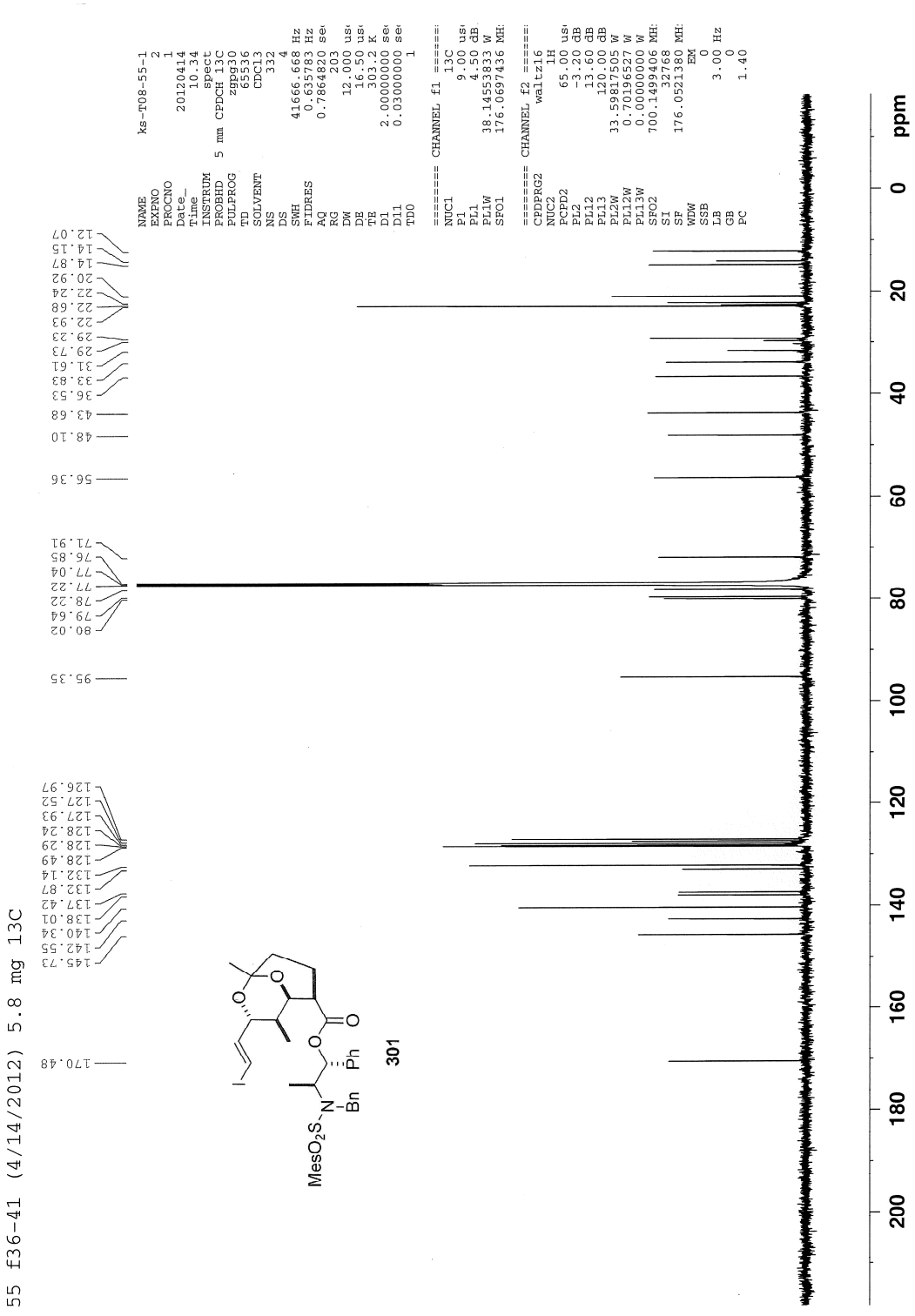

33 f6-11 (11/18/2009) 10.7 mg
Current Data Parameters
NAME Ks-704-33-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091118
Time 2.44
INSTRUM DPX400
PROBHD 5 mm BBO BZ-H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559040 sec
RG 406.4
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
PMP
Ph
MesO2S
N
Bn
OH
298
ppm

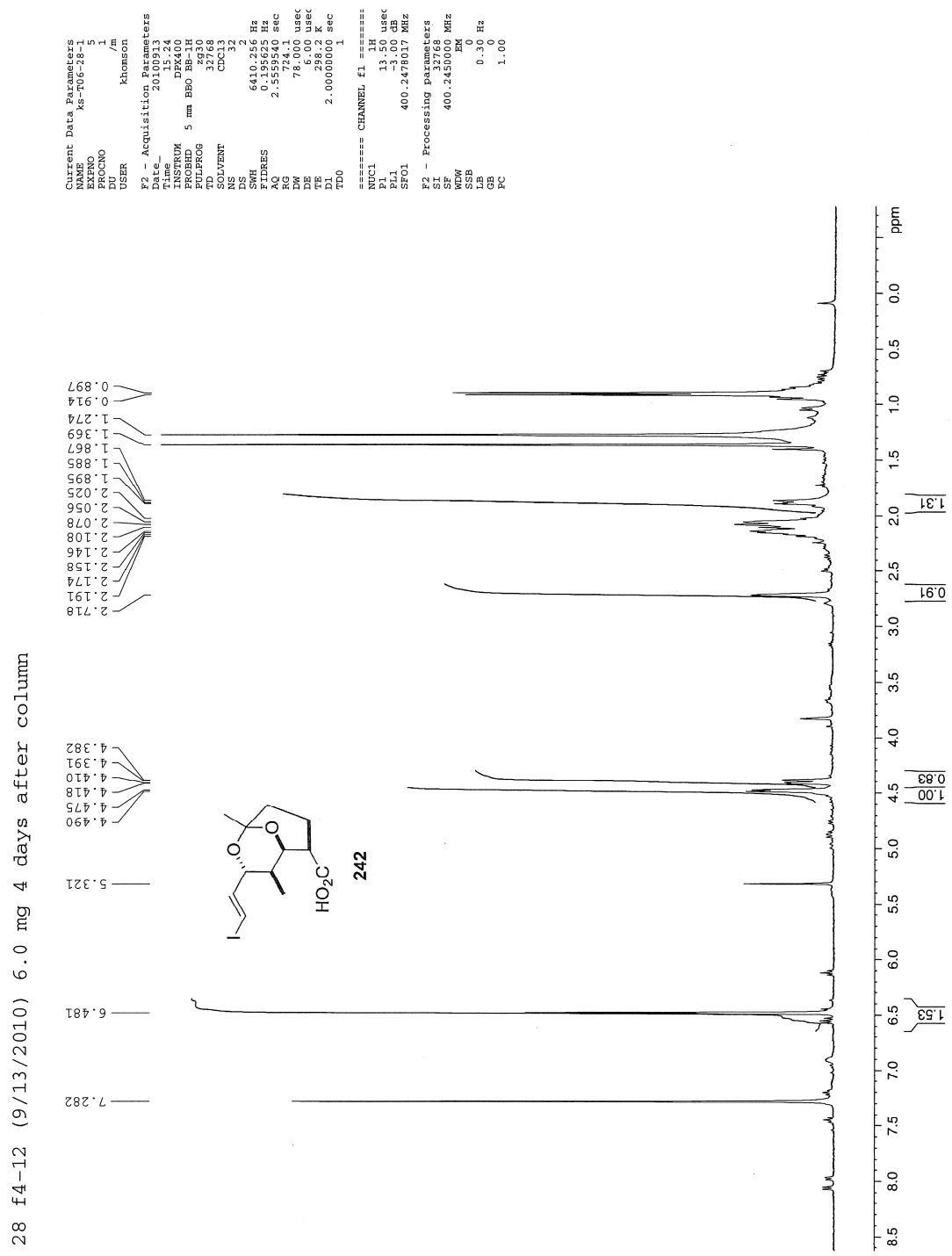

33 f6-11 (11/18/2009) 10.7 13C 9 hr
NAME ks-T04-33-1
EXPNO 11
PROCNO 1
Date_ 20091119
Time 7.46
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 9216
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 9195.2
DW 20.850 u
DE 6.00 u
TE 298.2 K
D1 2.00000000 s
d11 0.03000000 s
DELTA 1.89999998 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 8.30 u
PL1 -3.00 d
SFO1 100.6517495 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 -3.00 d
PL12 15.00 d
PL13 15.00 d
SFO2 400.2466010 M
SI 32768
SF 100.6416850 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
PMP
Ph
Bn
MesO2S
OH
298
ppm

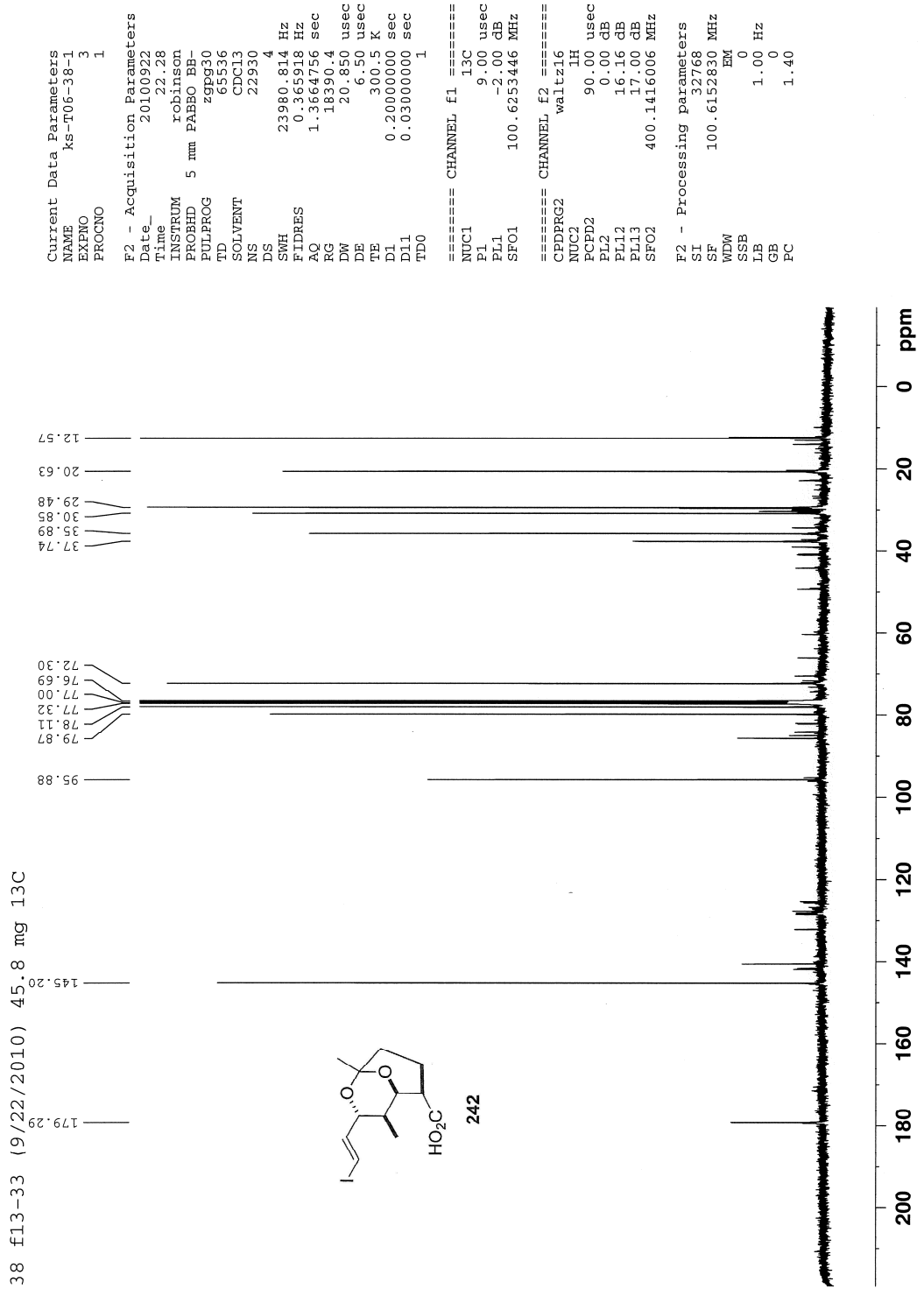

42 f4-13 (12/6/2009) 5.8 mg
Current Data Parameters
NAME ks-T04-43-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091207
Time 12.16
INSTRUN DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55595540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
PMP
Ph
Bn
MesO2S
299
ppm
12.25
1.69
2.61
3.98
2.47
1.04
2.55
1.10
1.00
4.11
1.21
3.80
1.16
12.33
1.35
3.67
7.56
5.68
2.97
4.19
6.58
2.02
4.27
4.04

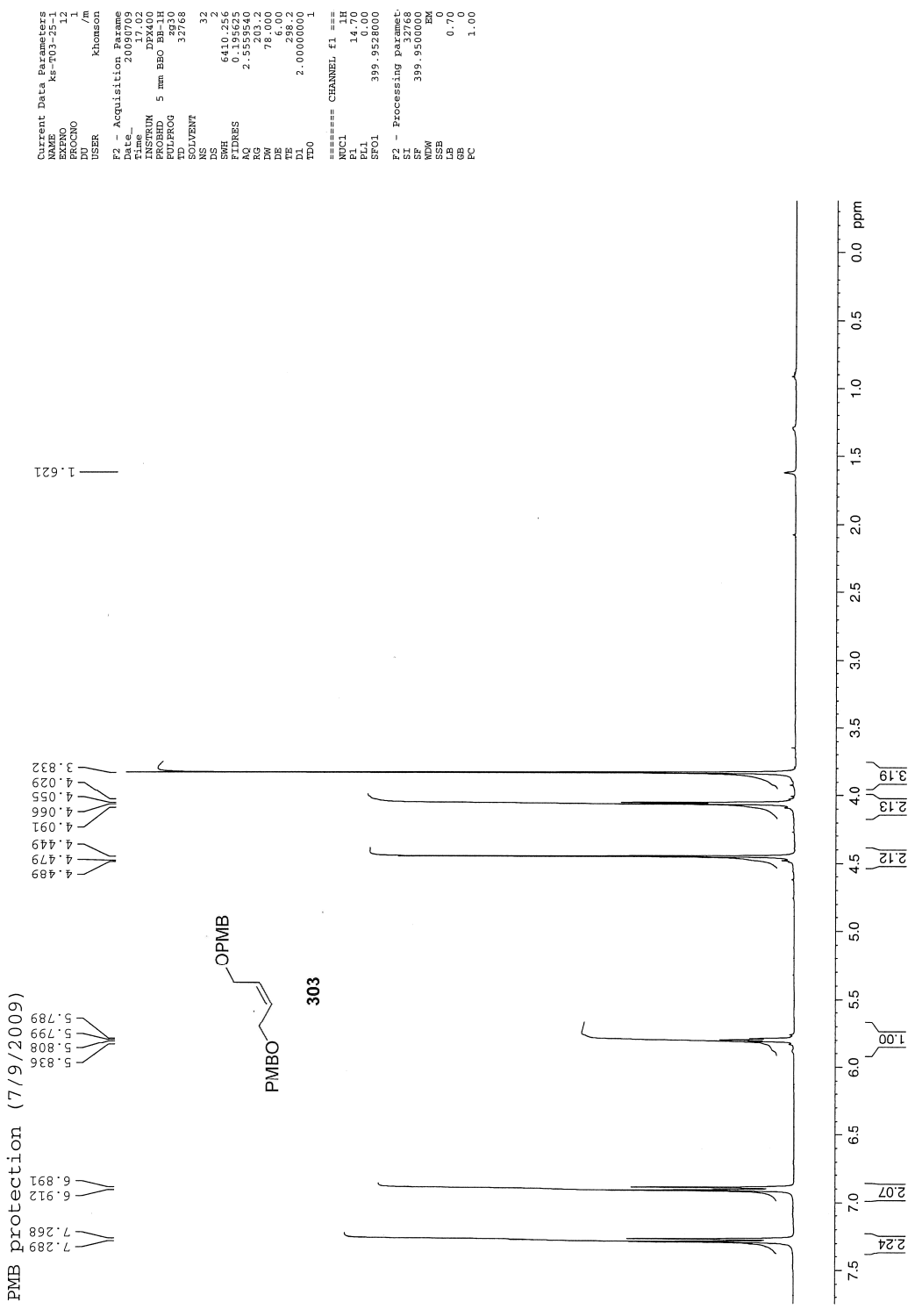

42 f4-13 (12/6/2009) 5.8 mg 13C
Current Data Parameters
NAME ks-T04-43-1
EXPNO 4
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20091207
Time 22.18
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 5792.6
DW 20.850 u
DE 6.00 u
TE 296.2 K
D1 2.00000000 s
d11 0.03000000 s
DELTA 1.89999998 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 8.30 u
PL1 -3.00 d
SFO1 100.6517495 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 -3.00 d
PL12 15.00 d
PL13 15.00 d
SFO2 400.2466010 M
F2 - Processing parameter
SI 32768
SF 100.6416850 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
206.96
173.47
160.22
144.25
142.45
140.53
138.87
138.00
133.05
132.11
130.93
130.23
128.68
128.29
128.16
127.65
127.28
127.00
113.61
96.50
81.34
80.34
77.89
77.35
77.03
76.71
56.04
55.38
47.72
47.05
39.61
31.92
29.72
22.91
20.94
14.42
12.17
PMP
Ph
Bn
MesO2S
299
ppm

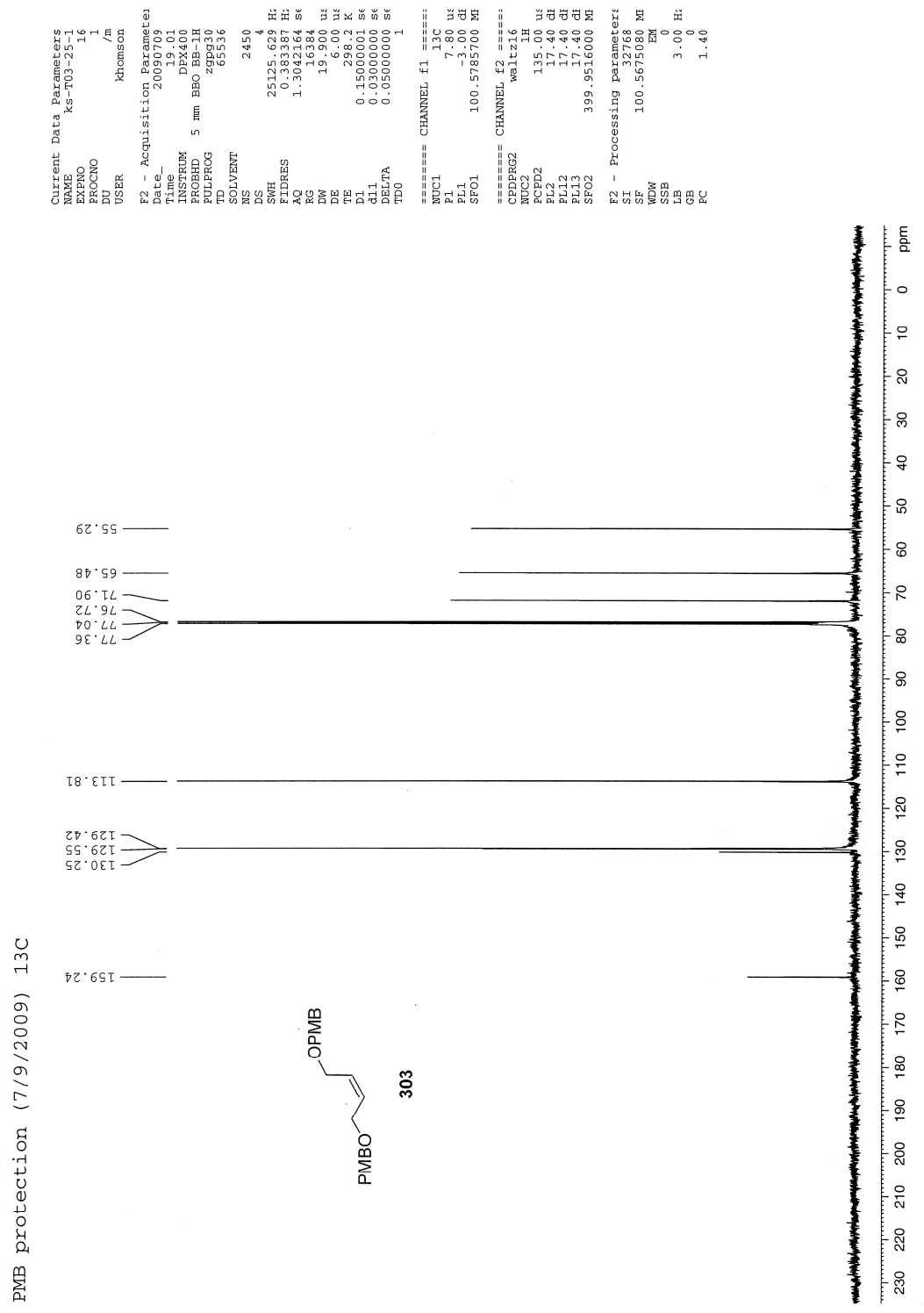

55 f36-41 (4/14/2012) 5.8 mg
NAME ks-T08-55-1
EXPNO 1
PROCNO 1
Date_ 20120414
Time_ 10.29
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 se
RG 36
DW 42.000 us
DE 6.50 us
TE 303.2 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 9.40 us
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MH
SI 131072
SF 700.1471400 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
301
ppm

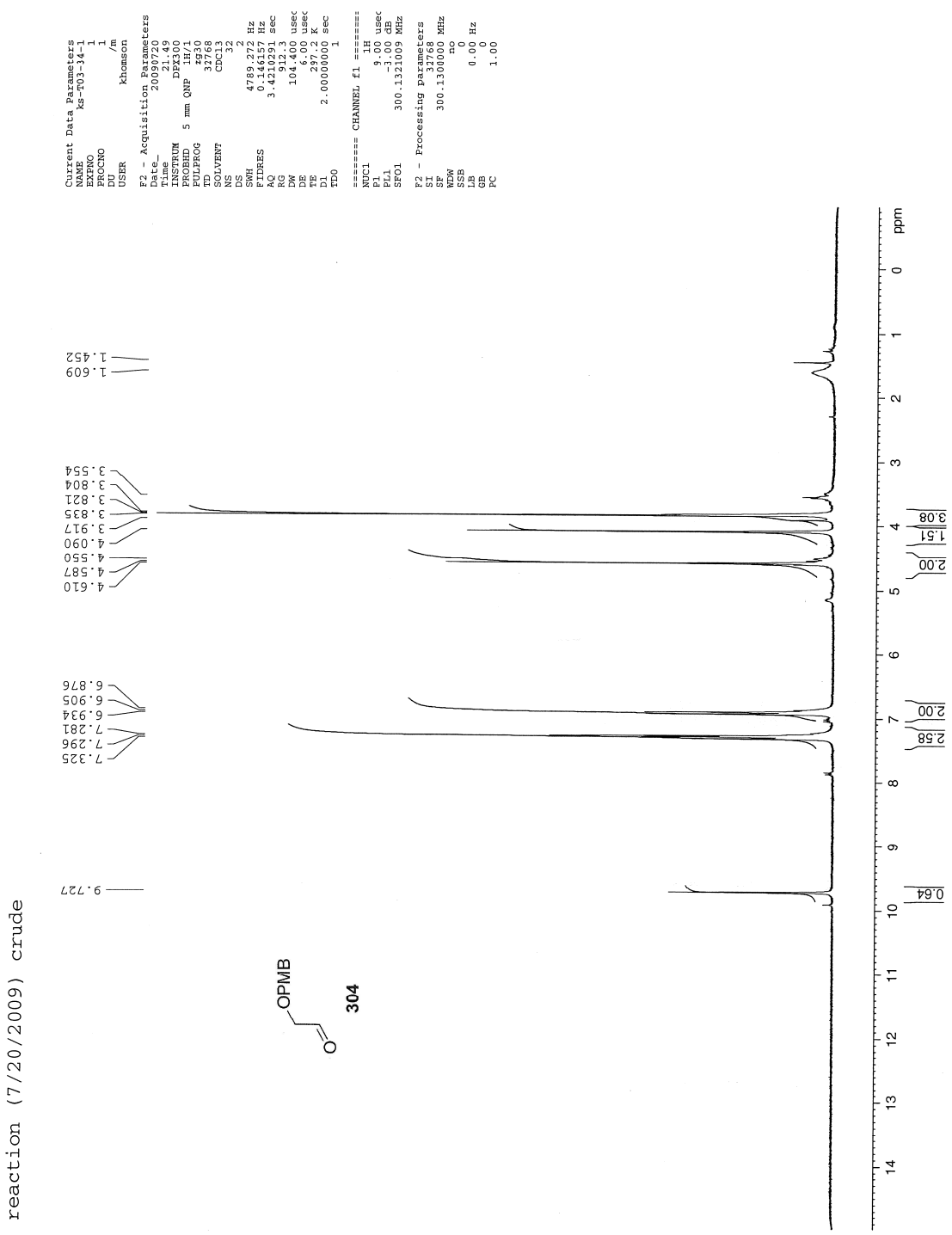

55 f36-41 (4/14/2012) 5.8 mg 13C
ks-T08-55-1
ppm
MesO2S
N
Bn
Ph
O
I
301

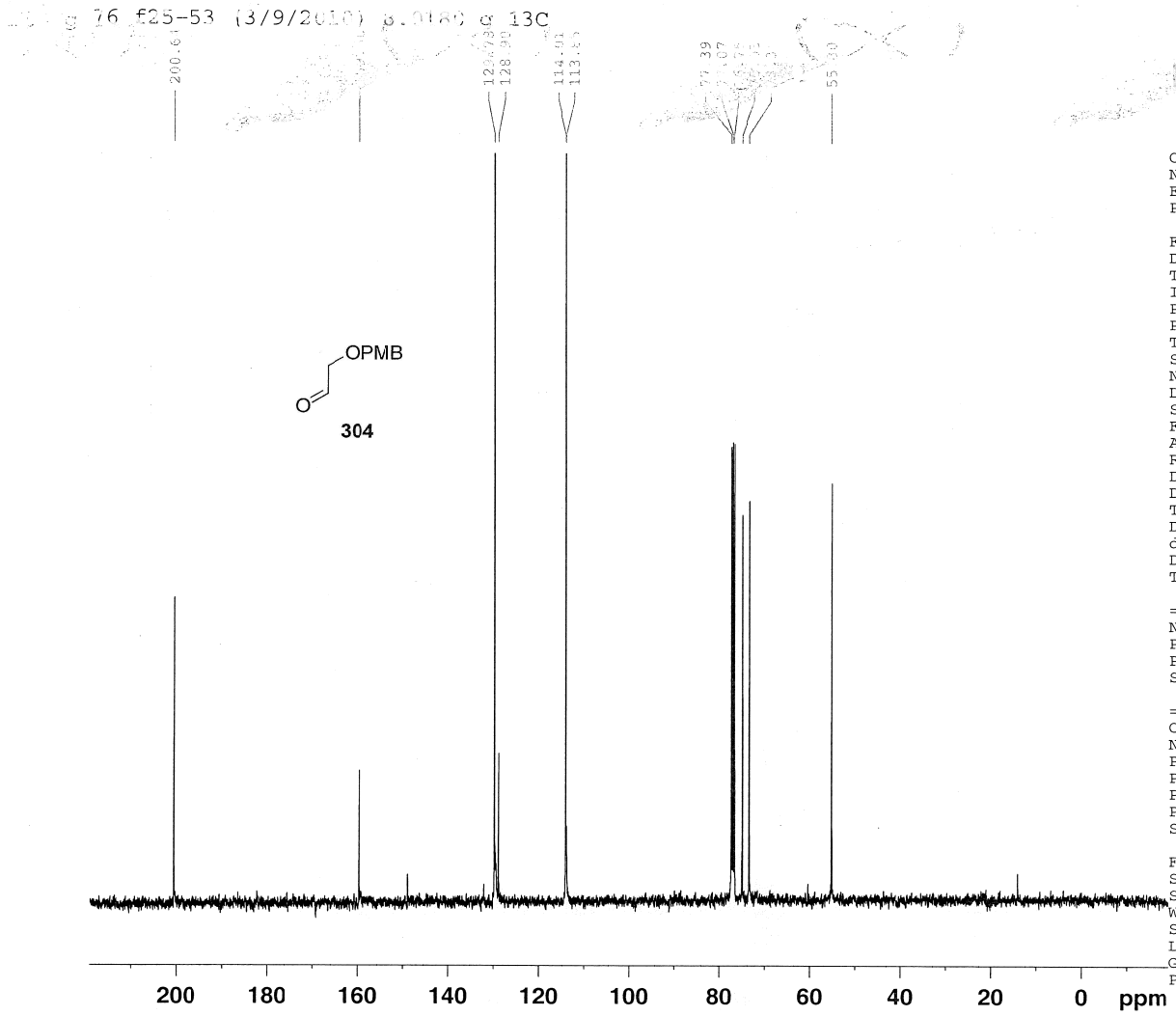

28 f4-12 (9/13/2010) 6.0 mg 4 days after column
Current Data Parameters
NAME ks-T06-28-1
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100913
Time 15.24
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55559540 sec
RG 7241.1
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.55 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
0.897
0.914
1.274
1.369
1.867
1.885
1.895
2.025
2.056
2.078
2.108
2.146
2.158
2.174
2.191
2.718
4.382
4.391
4.410
4.418
4.475
4.490
5.321
6.481
7.282
242
HO2C
1.31
0.91
0.83
1.00
1.53
ppm


38 f13-33 (9/22/2010) 45.8 mg 13C
Current Data Parameters
NAME ks-T06-38-1
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100922
Time 22.28
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 18390.4
DW 20.850 usec
DE 6.50 usec
TE 300.5 K
D1 0.20000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 -2.00 dB
SFO1 100.6253446 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 16.16 dB
PL13 17.00 dB
SFO2 400.1416006 MHz
F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
179.29
145.20
95.88
79.87
78.11
77.32
77.00
76.69
72.30
37.74
35.89
30.85
29.48
20.63
12.57
HO2C
242
200
180
160
140
120
100
80
60
40
20
0
ppm


PMB protection (7/9/2009)
Current Data Parameters
NAME ks-f03-25-1
EXPNO 12
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parame
Date_ 20091709
Time 17.00
INSTRUN DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 203.2
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing paramet
SI 32768
SF 399.9500000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
1.621
3.832
4.029
4.055
4.066
4.091
4.449
4.479
4.489
5.789
5.799
5.808
5.836
6.891
6.912
7.268
7.289
OPMB
PMBO
303
3.19
2.13
2.12
1.00
2.07
2.24
ppm


PMB protection (7/9/2009) 13C
Current Data Parameters
NAME ks-T03-25-1
EXPNO 16
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20090709
Time 19.01
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
159.24
130.25
129.55
129.42
113.81
77.36
77.04
76.72
71.90
65.48
55.29
OPMB
PMBO
303
ppm


reaction (7/20/2009) crude
Current Data Parameters
NAME Ks-F03-34-1
EXPNO 1
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090720
Time 21.49
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4211291 sec
RG 203.3
DW 104.400 usec
DE 6.00 usec
TE 297.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
9.727
7.325
7.296
7.281
6.934
6.905
6.876
4.610
4.587
4.550
4.090
3.917
3.835
3.821
3.804
3.554
1.609
1.452
OPMB
O
304
0.64
2.58
2.00
2.00
1.51
3.08
ppm



BRUKER

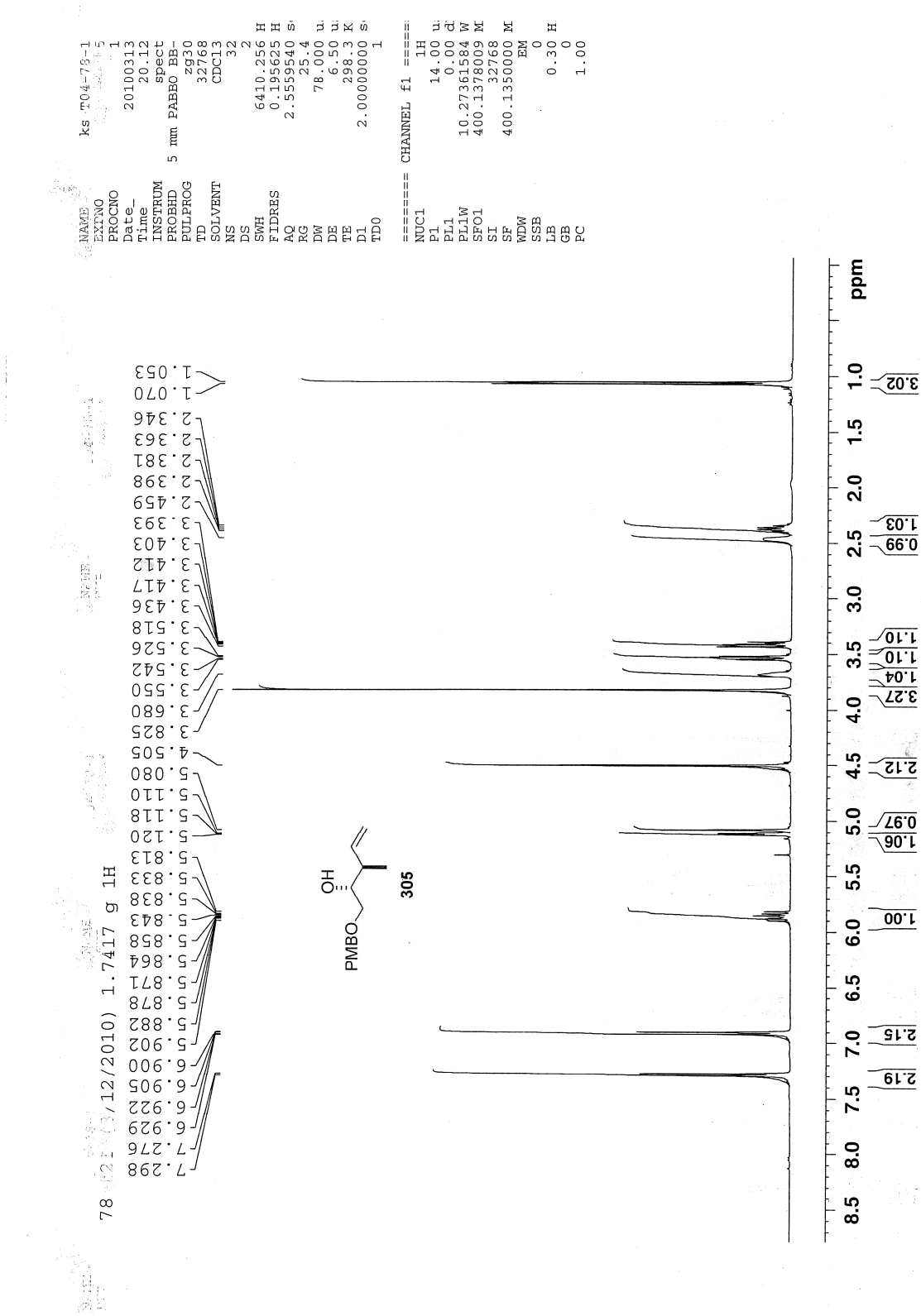
Current Data Parameters
NAME ks-T04-76-1
EXPNO 8
PROCNO 1

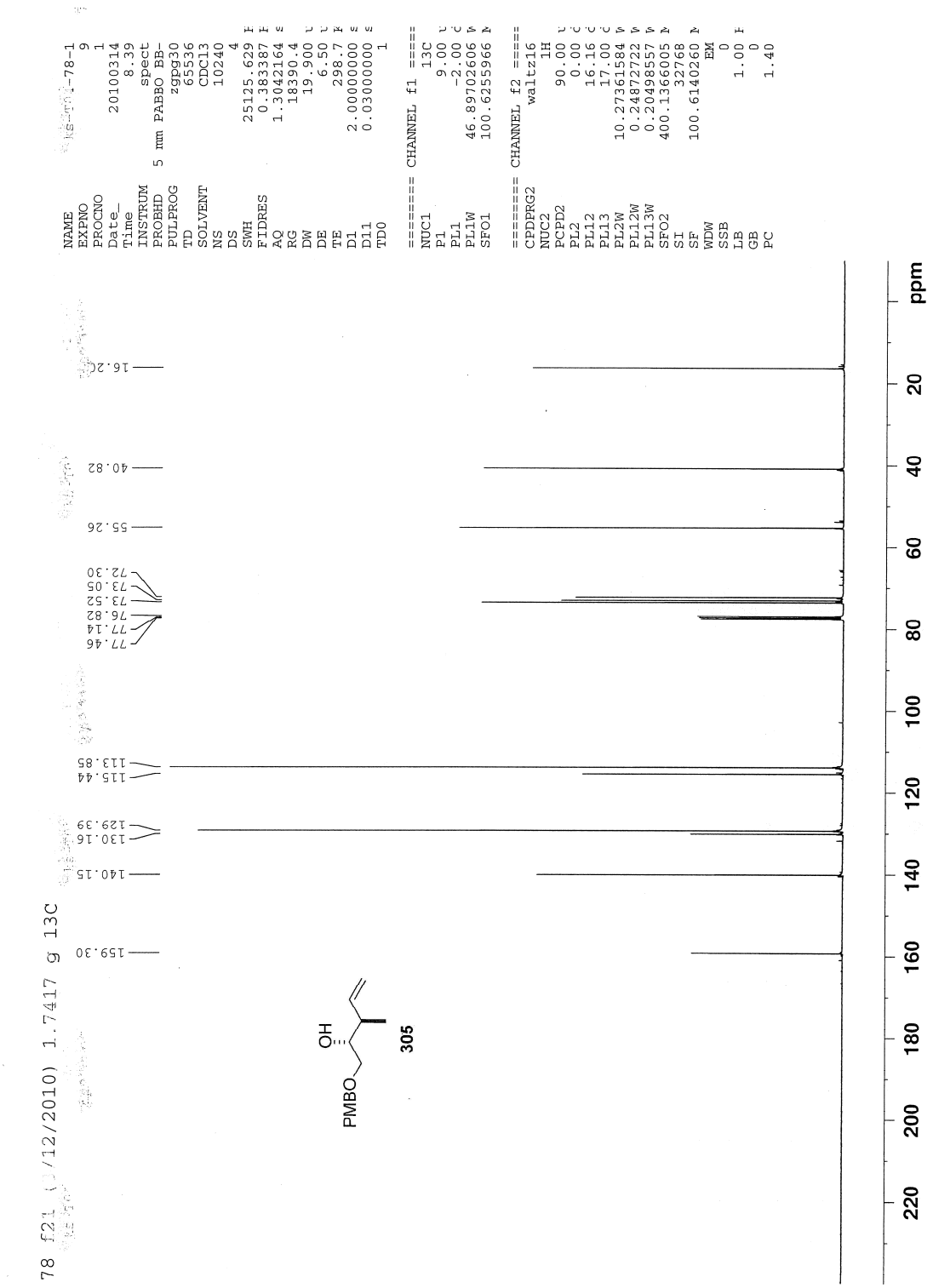
F2 - Acquisition Parameters
Date_ 20100309
Time 15.58
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 368
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 4597.6
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

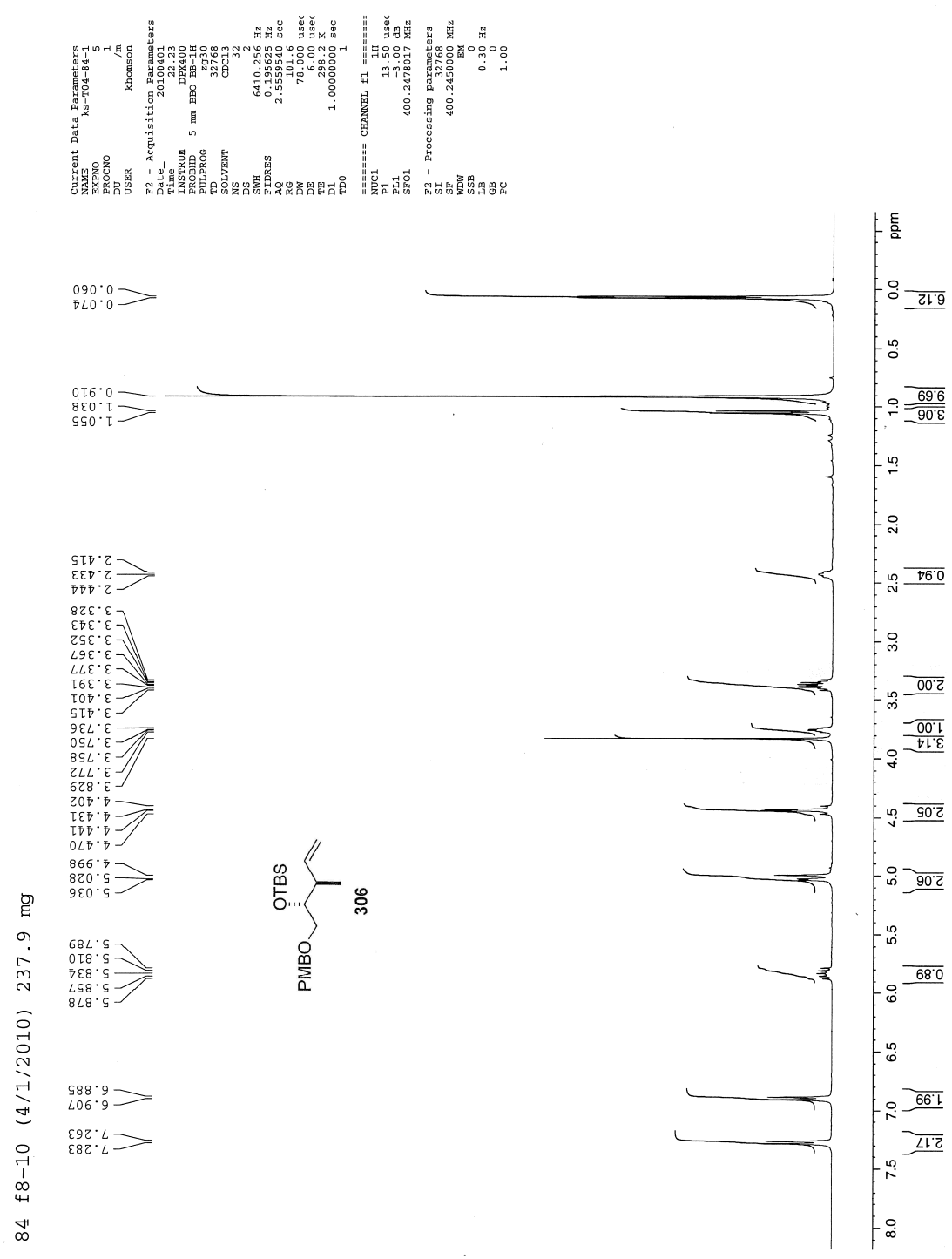
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz

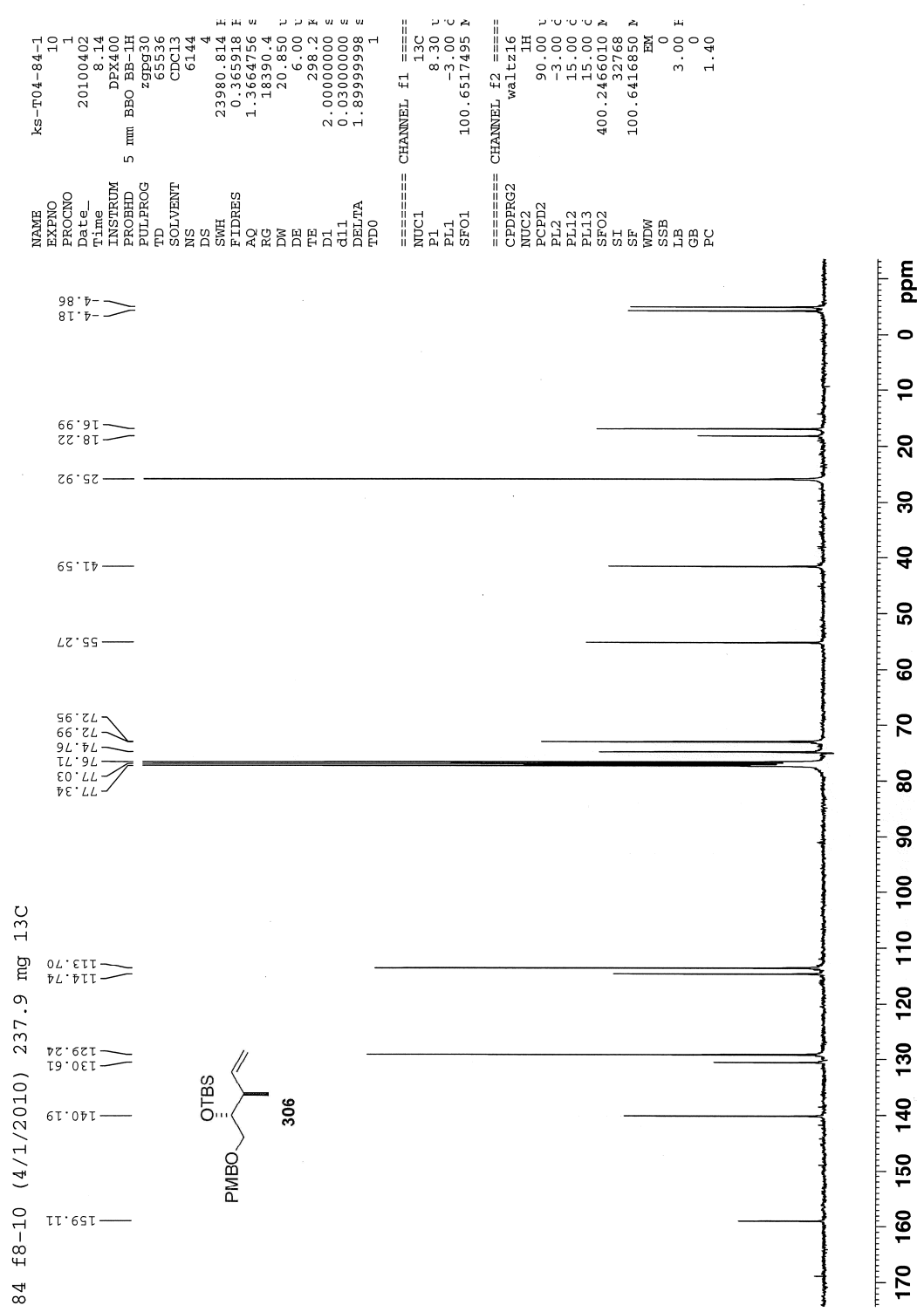
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz

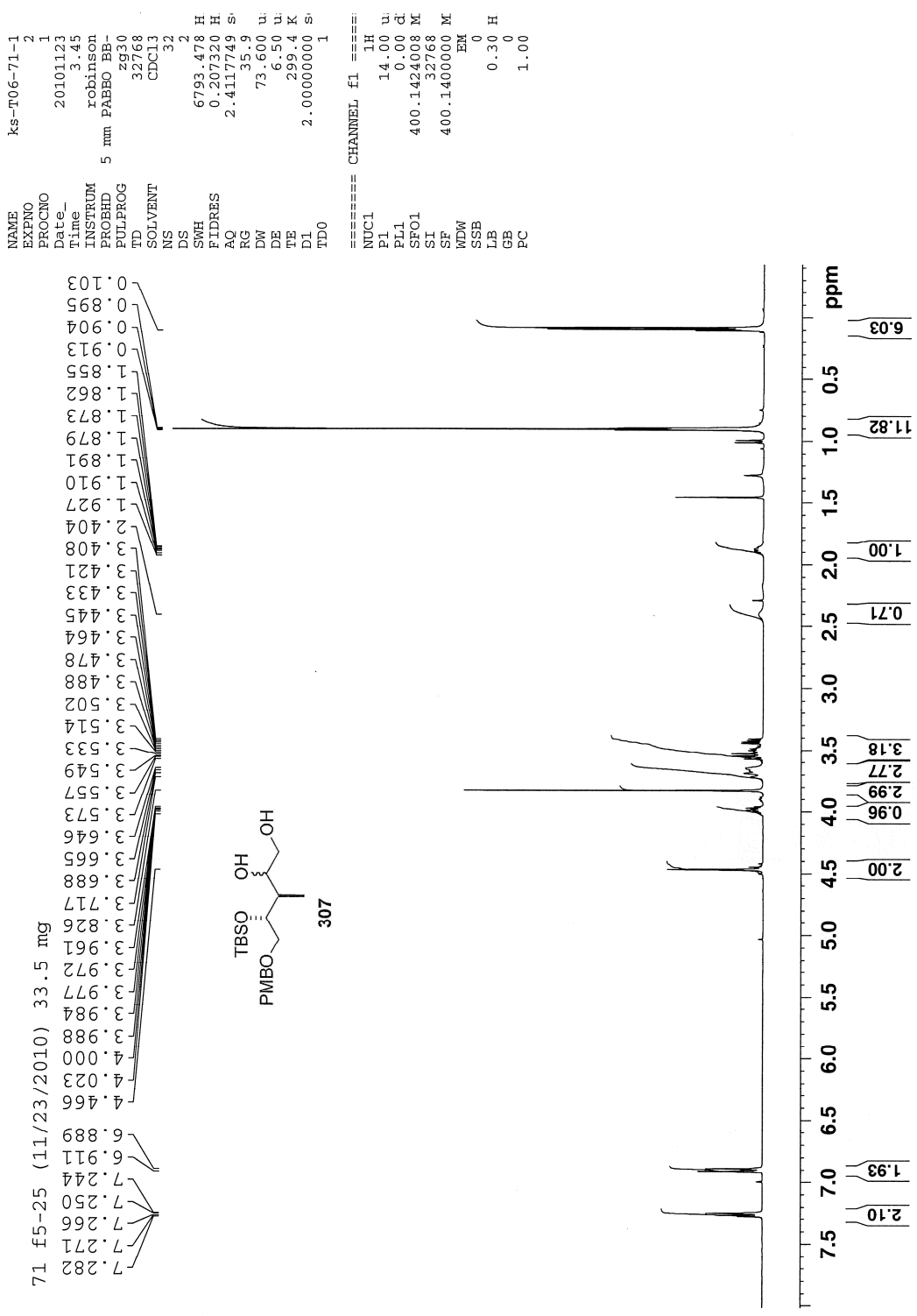
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

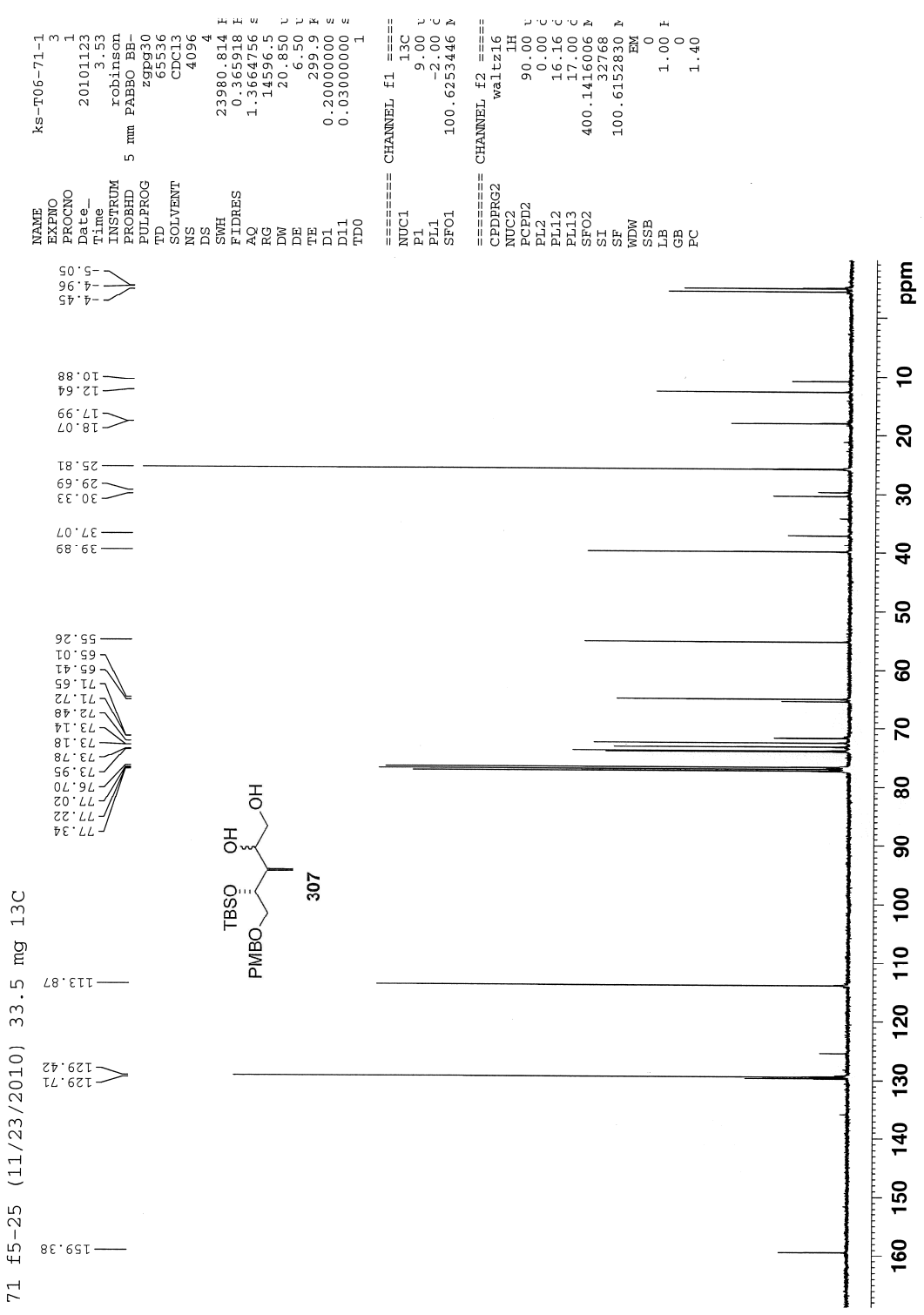

NAME ks T04-78-1
EXTNO 5
PROCNO 1
Date_ 20100313
Time_ 20.12
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 25.4
DW 78.000 u
DE 6.50 u
TE 298.3 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1378009 M
SI 32768
SF 400.1350000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
78 ks T04-78-1 (3/12/2010) 1.7417 g 1H
7.298
7.276
6.929
6.922
6.905
6.900
5.902
5.882
5.878
5.871
5.864
5.858
5.843
5.838
5.833
5.813
5.120
5.118
5.110
5.080
4.505
3.825
3.680
3.550
3.542
3.526
3.518
3.436
3.417
3.412
3.403
3.393
2.459
2.398
2.381
2.363
2.346
1.070
1.053
OH
PMBO
305
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
2.19
2.15
1.00
1.06
0.97
2.12
3.27
1.04
1.10
1.10
0.99
1.03
3.02

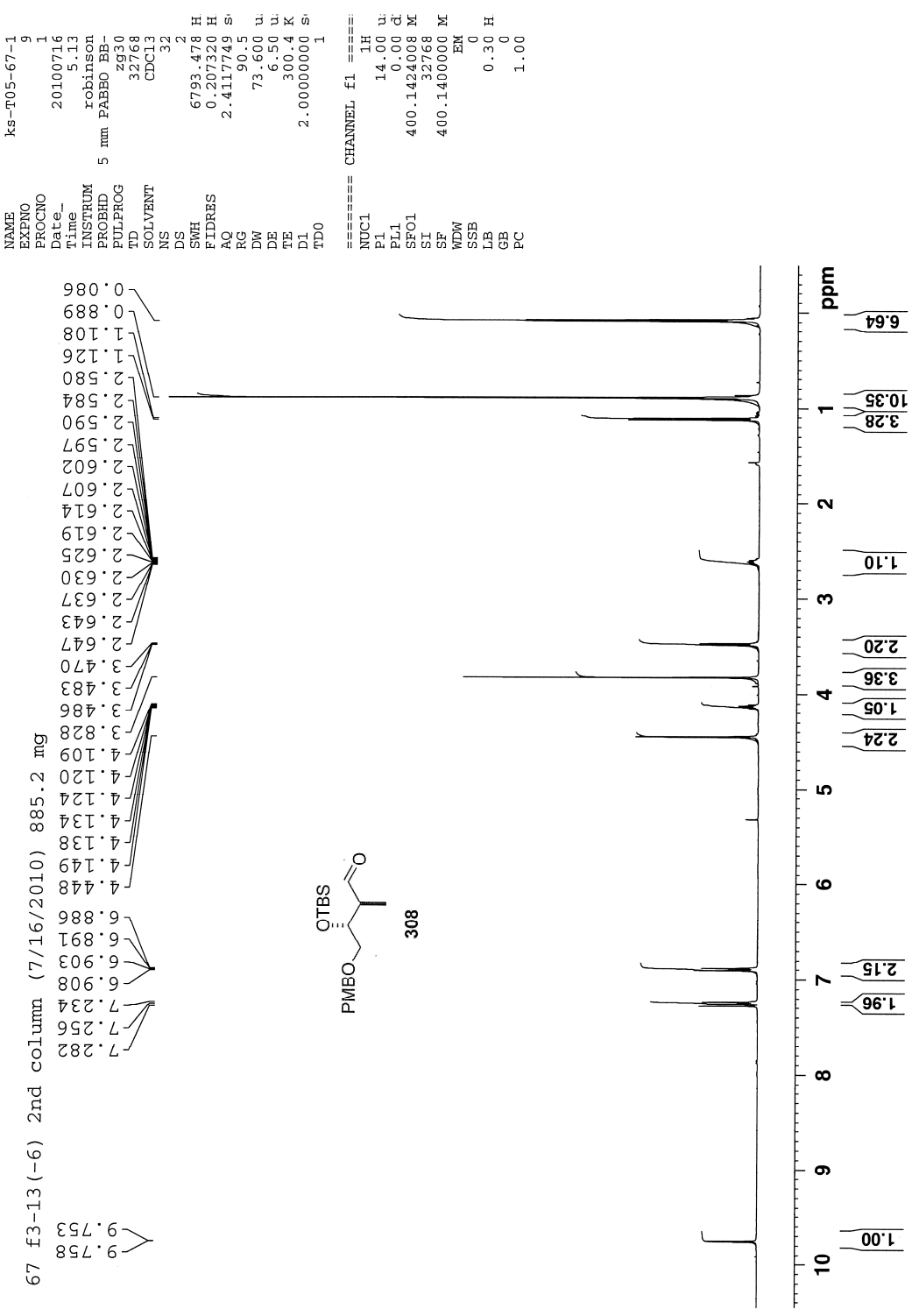

78 f21 (12/2010) 1.7417 g 13C
NAME KS-01-1-78-1
EXPNO 9
PROCNO 1
Date_ 20100314
Time 8.39
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 18390.4
DW 19.900 u
DE 6.50 u
TE 298.7 K
D1 2.00000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
PL1W 46.89702606 W
SFO1 100.6255966 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1366005 M
SI 32768
SF 100.6140260 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
16.20
40.82
55.26
72.30
73.05
73.52
76.82
77.14
77.46
113.85
115.44
129.39
130.16
140.15
159.30
OH
PMBO
305
220
200
180
160
140
120
100
80
60
40
20
ppm

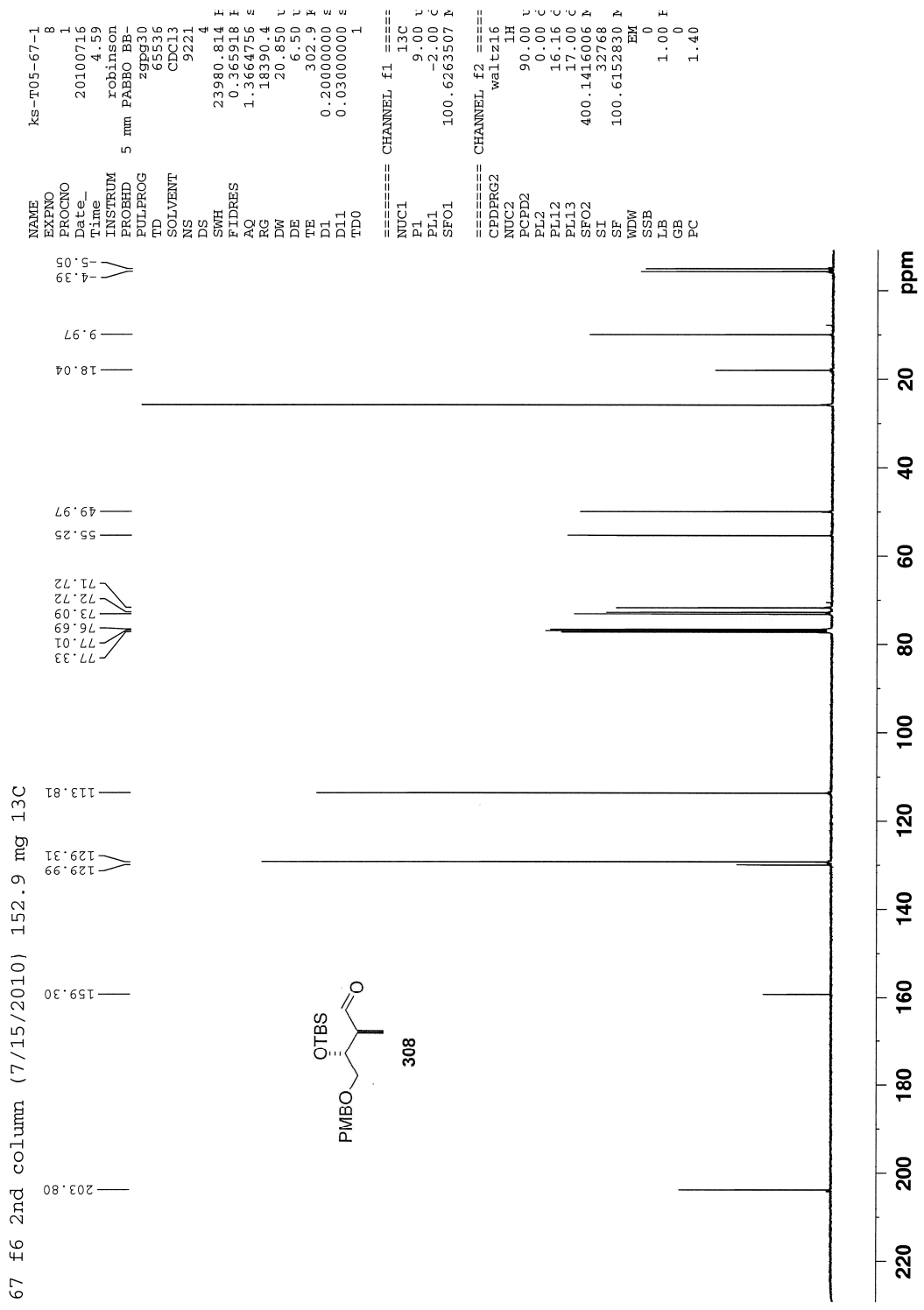

84 f8-10 (4/1/2010) 237.9 mg
Current Data Parameters
NAME ks-f04-84-1
EXPNO 5
PROCNO 1
DU /m
USER khomson
P2 - Acquisition Parameters
Date_ 20100401
Time 10.23
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 101.6
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTBS
PMBO
306
ppm

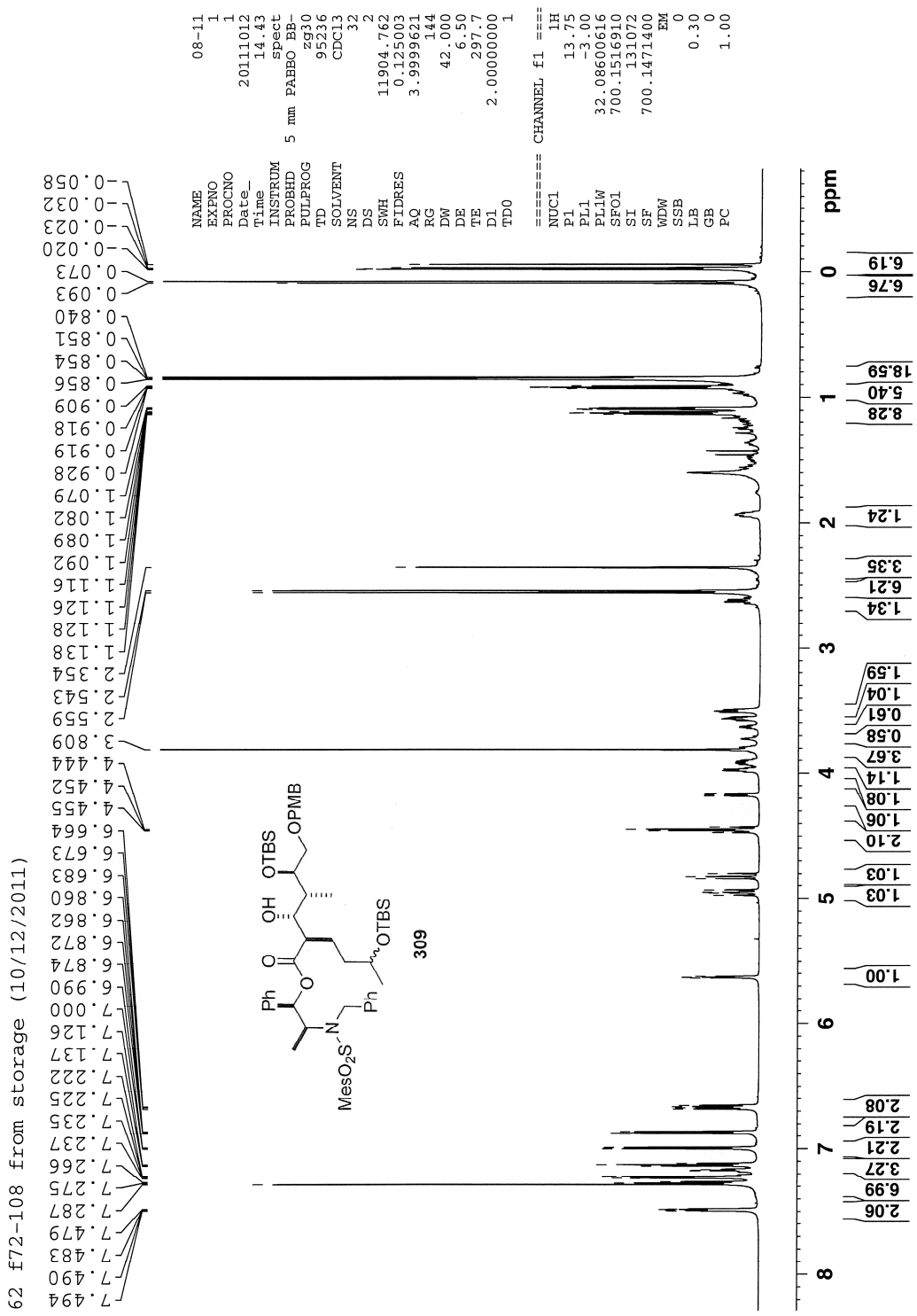

84 f8-10 (4/1/2010) 237.9 mg 13C
NAME ks-T04-84-1
EXPNO 10
PROCNO 1
Date_ 20100402
Time_ 8.14
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 6144
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 18390.4
DW 20.850 u
DE 6.00 u
TE 298.2 K
D1 2.00000000 s
d11 0.03000000 s
DELTA 1.89999998 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 8.30 u
PL1 -3.00 d
SFO1 100.6517495 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 -3.00 d
PL12 15.00 d
PL13 15.00 d
SFO2 400.2466010 M
SI 32768
SF 100.6416850 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
-4.86
-4.18
16.99
18.22
25.92
41.59
55.27
72.95
72.99
74.76
76.71
77.03
77.34
113.70
114.74
129.24
130.61
140.19
159.11
OTBS
PMBO
306
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

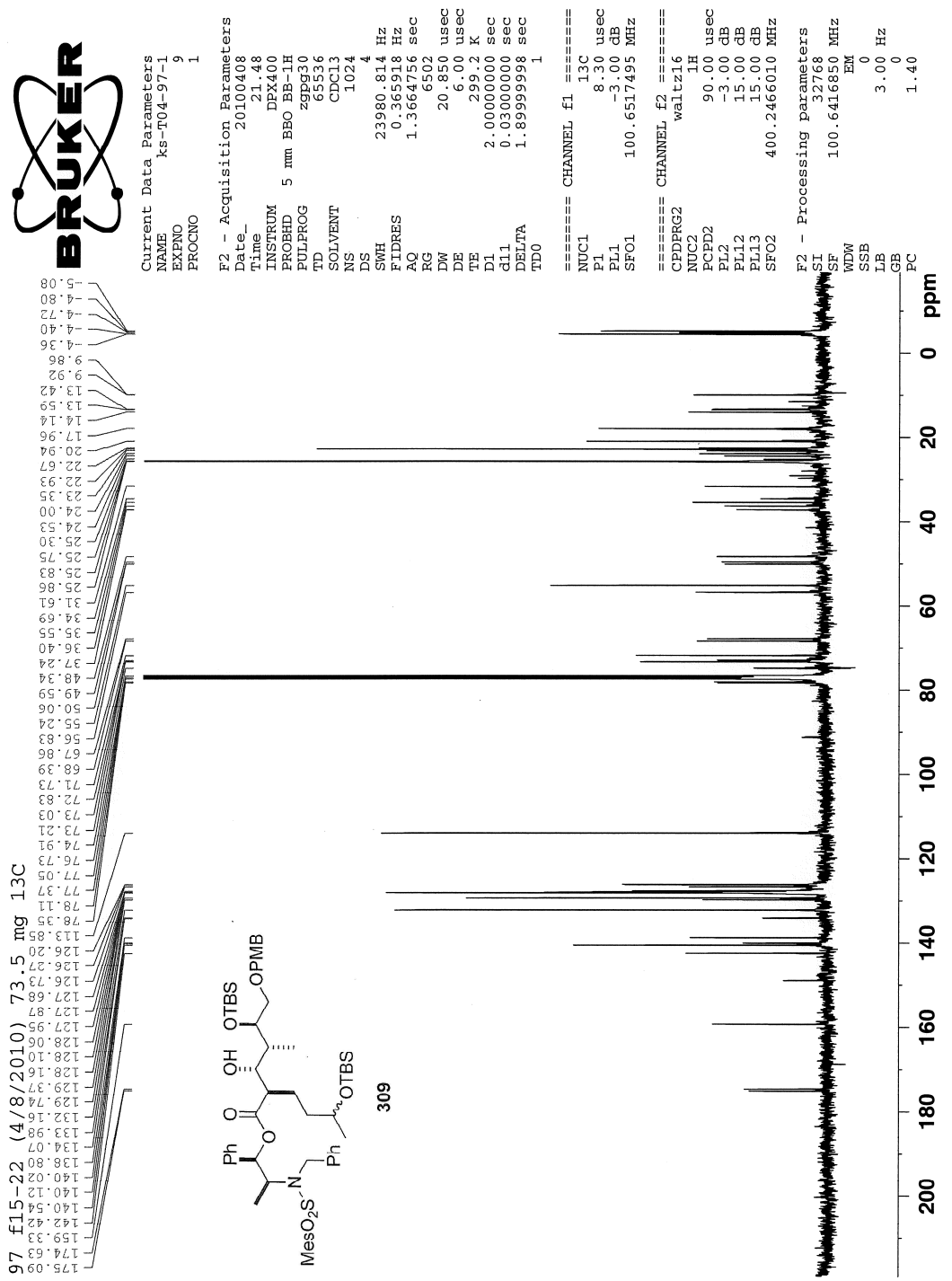

NAME ks-T06-71-1
EXPNO 2
PROCNO 1
Date_ 20101123
Time 3.45
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 35.9
DW 73.600 u
DE 6.50 u
TE 299.4 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
71 f5-25 (11/23/2010) 33.5 mg
TBSO
OH
OH
PMBO
307
ppm
6.03
11.82
1.00
0.71
3.18
2.77
2.99
0.96
2.00
1.93
2.10

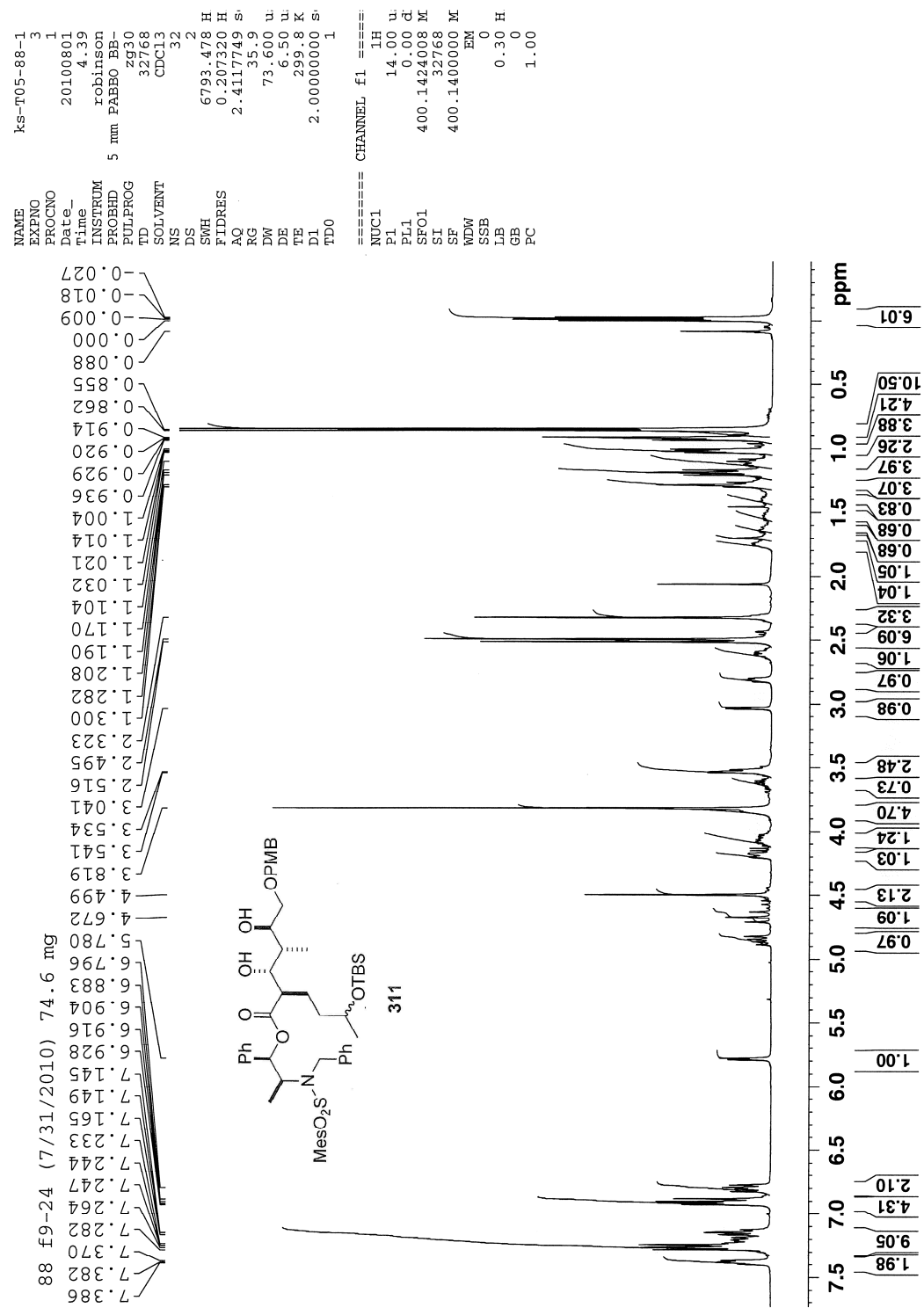

71 f5-25 (11/23/2010) 33.5 mg 13C
NAME ks-T06-71-1
EXPNO 3
PROCNO 1
Date_ 20101123
Time 3.53
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4096
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 14596.5
DW 20.850 u
DE 6.50 u
TE 299.9 K
D1 0.20000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 9.00 u
PL1 -2.00 d
SFO1 100.6253446 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
SFO2 400.1416006 M
SI 32768
SF 100.6152830 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
-5.05
-4.96
-4.45
10.88
12.64
17.99
18.07
25.81
29.69
30.33
37.07
39.89
55.26
65.01
65.41
71.65
71.72
72.48
73.14
73.18
73.78
73.95
76.70
77.02
77.22
77.34
113.87
129.42
129.71
159.38
TBSO
OH
OH
PMBO
307
ppm

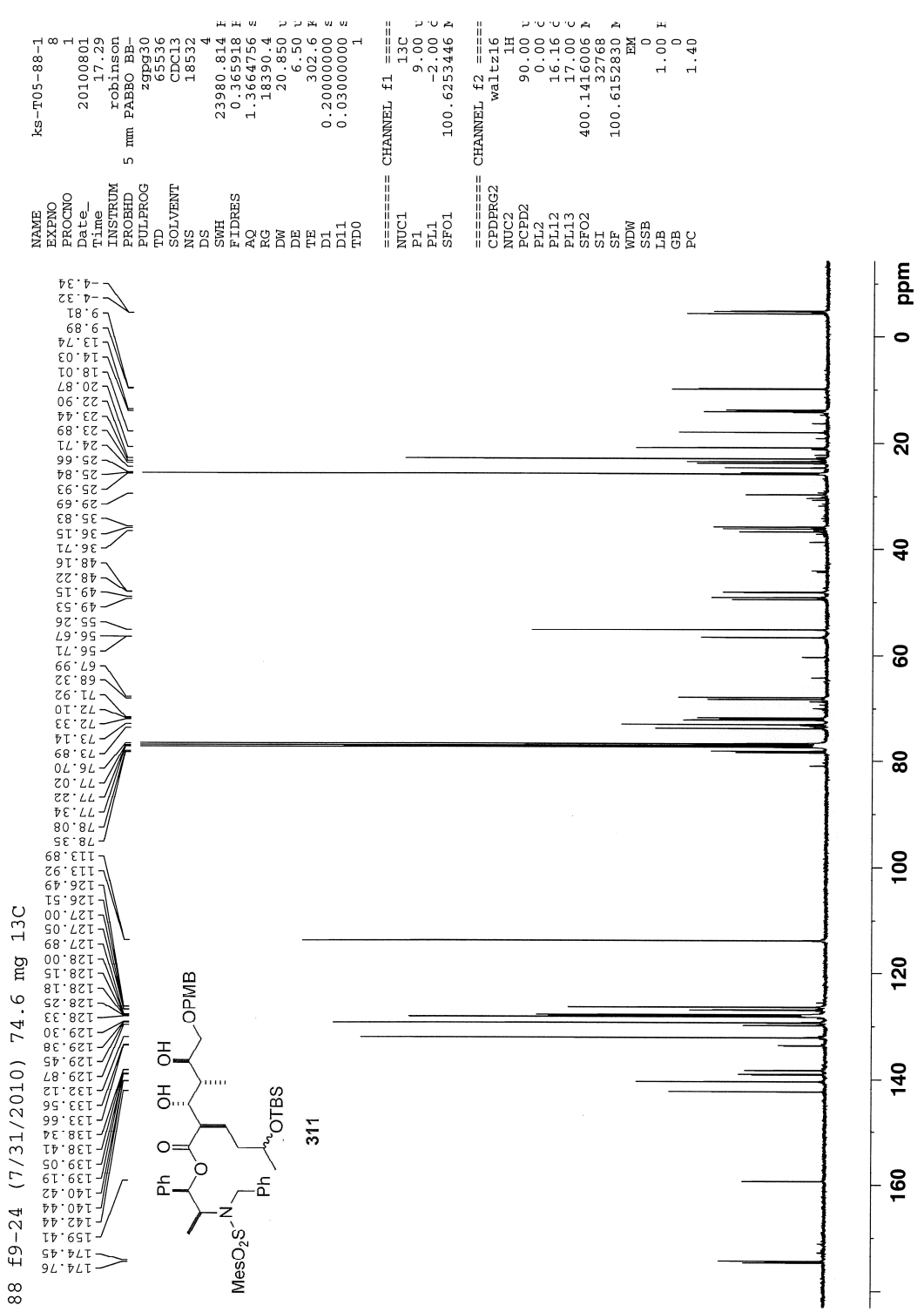

67 f3-13(-6) 2nd column (7/16/2010) 885.2 mg
9.758
9.753
7.282
7.256
7.234
6.908
6.903
6.891
6.886
4.448
4.149
4.138
4.134
4.124
4.120
4.109
3.828
3.486
3.483
3.470
2.647
2.643
2.637
2.630
2.625
2.619
2.614
2.607
2.602
2.597
2.590
2.584
2.580
1.126
1.108
0.889
0.086
PMBO
OTBS
308
NAME ks-T05-67-1
EXPNO 9
PROCNO 1
Date_ 20100716
Time_ 5.13
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 90.5
DW 73.600 u
DE 6.50 u
TE 300.4 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
ppm
1.00
1.96
2.15
2.24
1.05
3.36
2.20
1.10
10.35
3.28
6.64

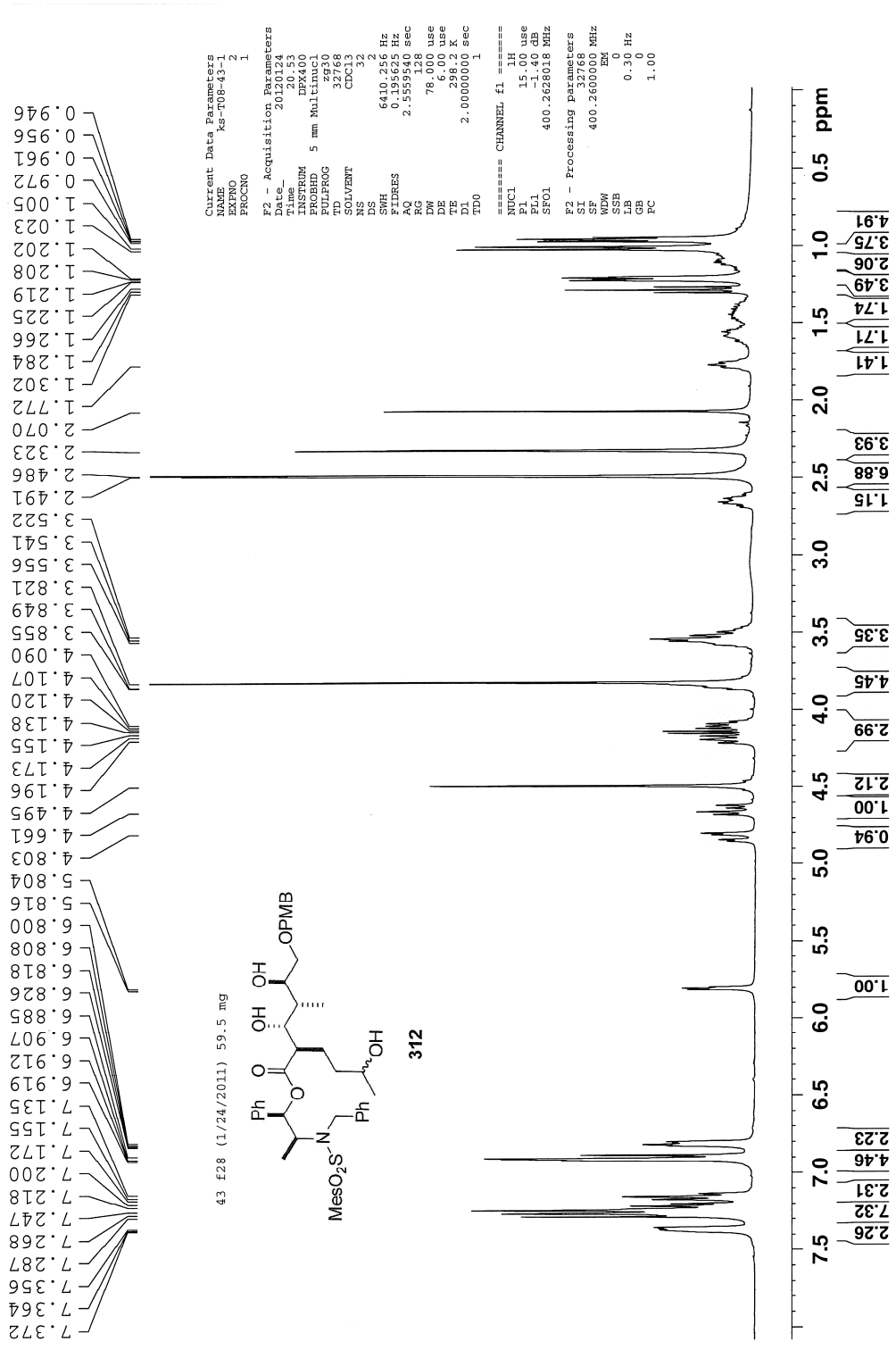

67 f6 2nd column (7/15/2010) 152.9 mg 13C
NAME ks-T05-67-1
EXPNO 8
PROCNO 1
Date_ 20100716
Time_ 4.59
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 9221
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 18390.4
DW 20.850 u
DE 6.50 u
TE 302.9 K
D1 0.20000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
SFO1 100.6263507 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
SFO2 400.1416006 M
SI 32768
SF 100.6152830 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
-5.05
-4.39
9.97
18.04
49.97
55.25
71.72
72.72
73.09
76.69
77.01
77.33
113.81
129.31
129.99
159.30
203.80
OTBS
PMBO
O
308
ppm
220
200
180
160
140
120
100
80
60
40
20

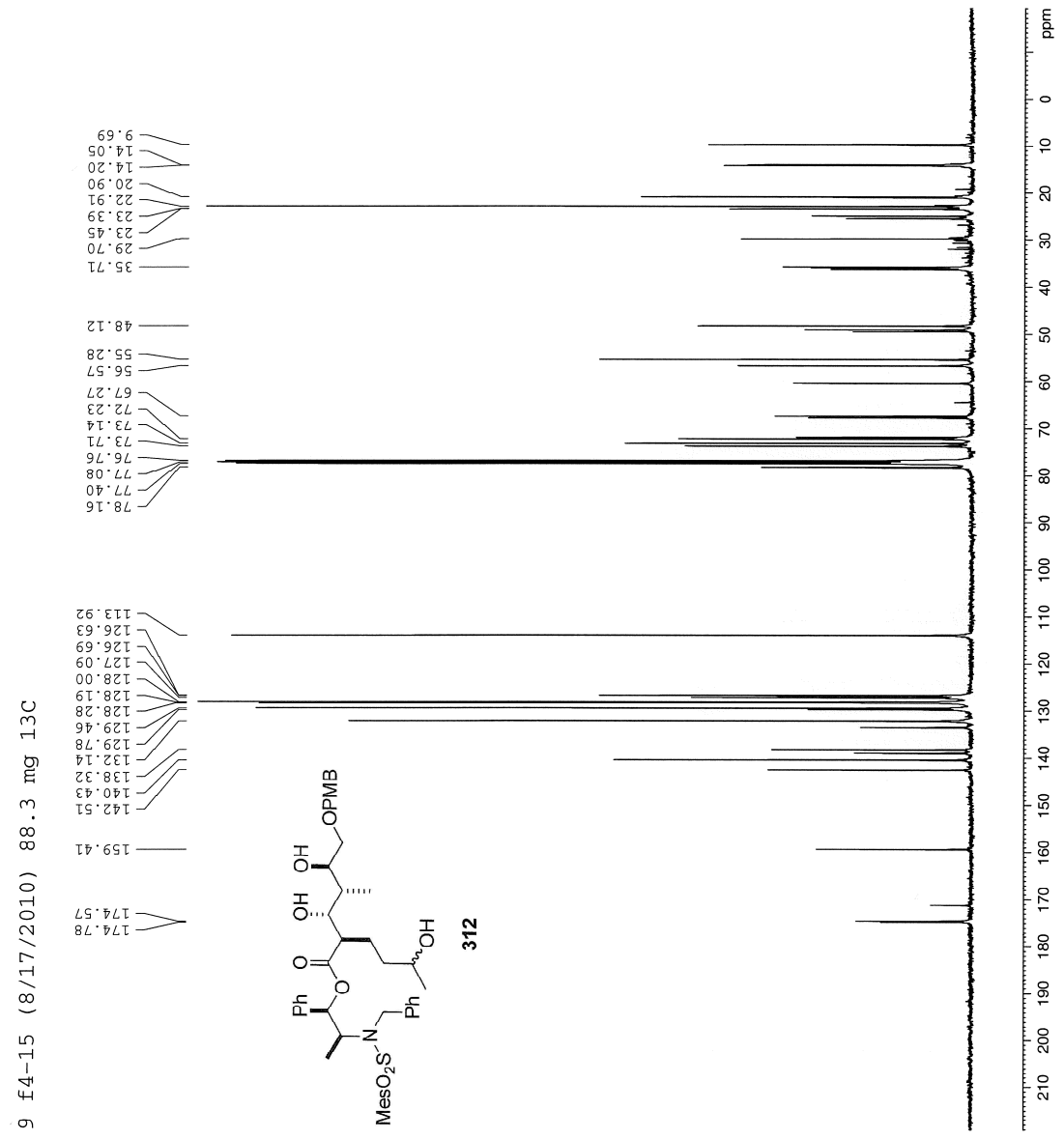

62 f72-108 from storage (10/12/2011)
309
Ph
O
OH
OTBS
OPMB
O
N
Ph
OTBS
MesO2S
NAME 08-11
EXPNO 1
PROCNO 1
Date_ 20111012
Time 14.43
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 32
DS 2
SWH 11904.762
FIDRES 0.125003
AQ 3.9999621
RG 144
DW 42.000
DE 6.50
TE 297.7
D1 2.00000000
TDO 1
======== CHANNEL f1 ====
NUC1 1H
P1 13.75
PL1 -3.00
PL1W 32.08600616
SFO1 700.1516910
SI 131072
SF 700.1471400
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
ppm

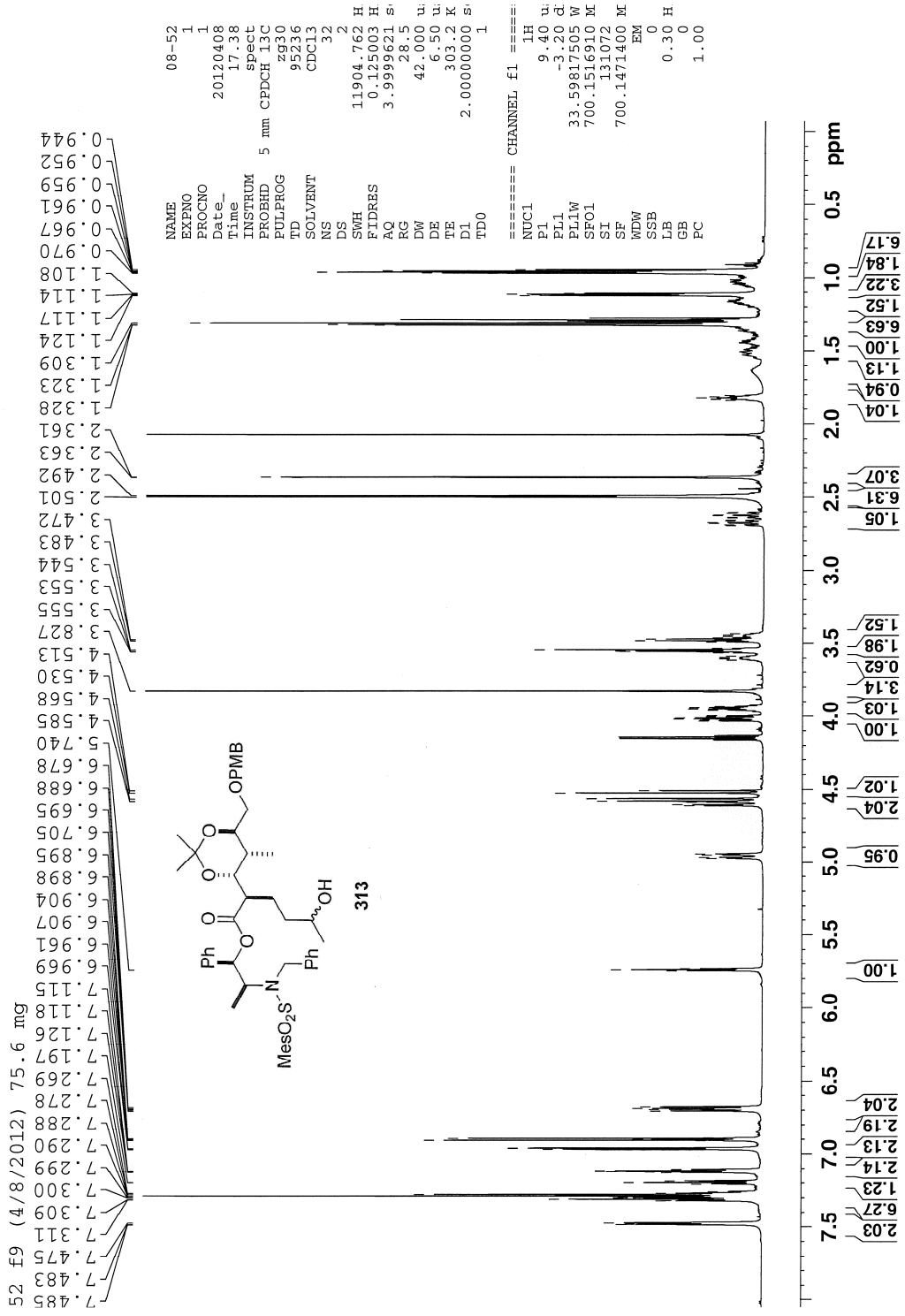

97 f15-22 (4/8/2010) 73.5 mg 13C
Current Data Parameters
NAME ks-T04-97-1
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100408
Time 21.48
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 6502
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
Ph
O
OH
OTBS
OPMB
O
O
N
MesO2S
Ph
OTBS
309
200
180
160
140
120
100
80
60
40
20
0
ppm

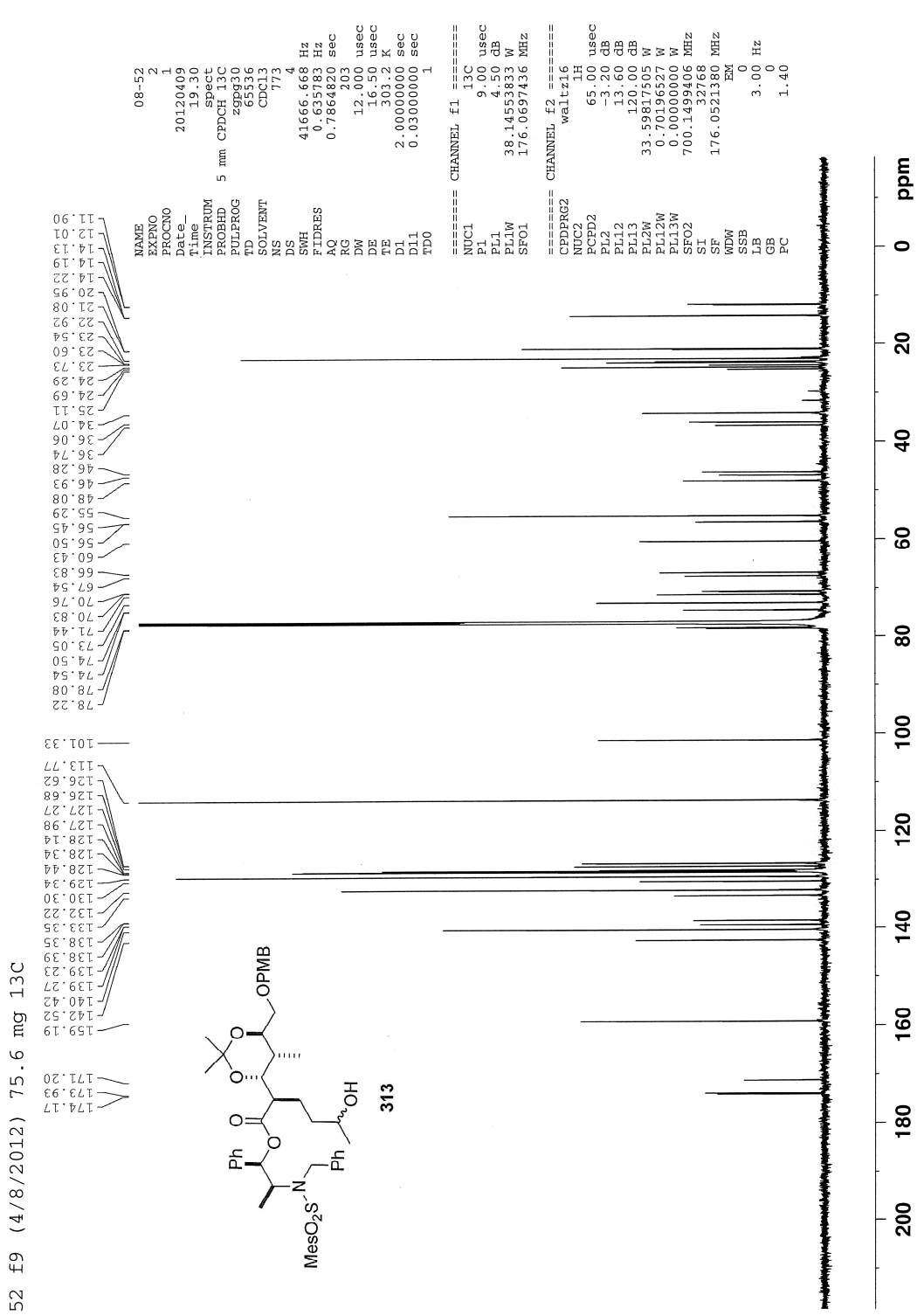

NAME ks-T05-88-1
EXPNO 3
PROCNO 1
Date_ 20100801
Time 4.39
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 35.9
DW 73.600 u
DE 6.50 u
TE 299.8 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
88 f9-24 (7/31/2010) 74.6 mg
311
ppm

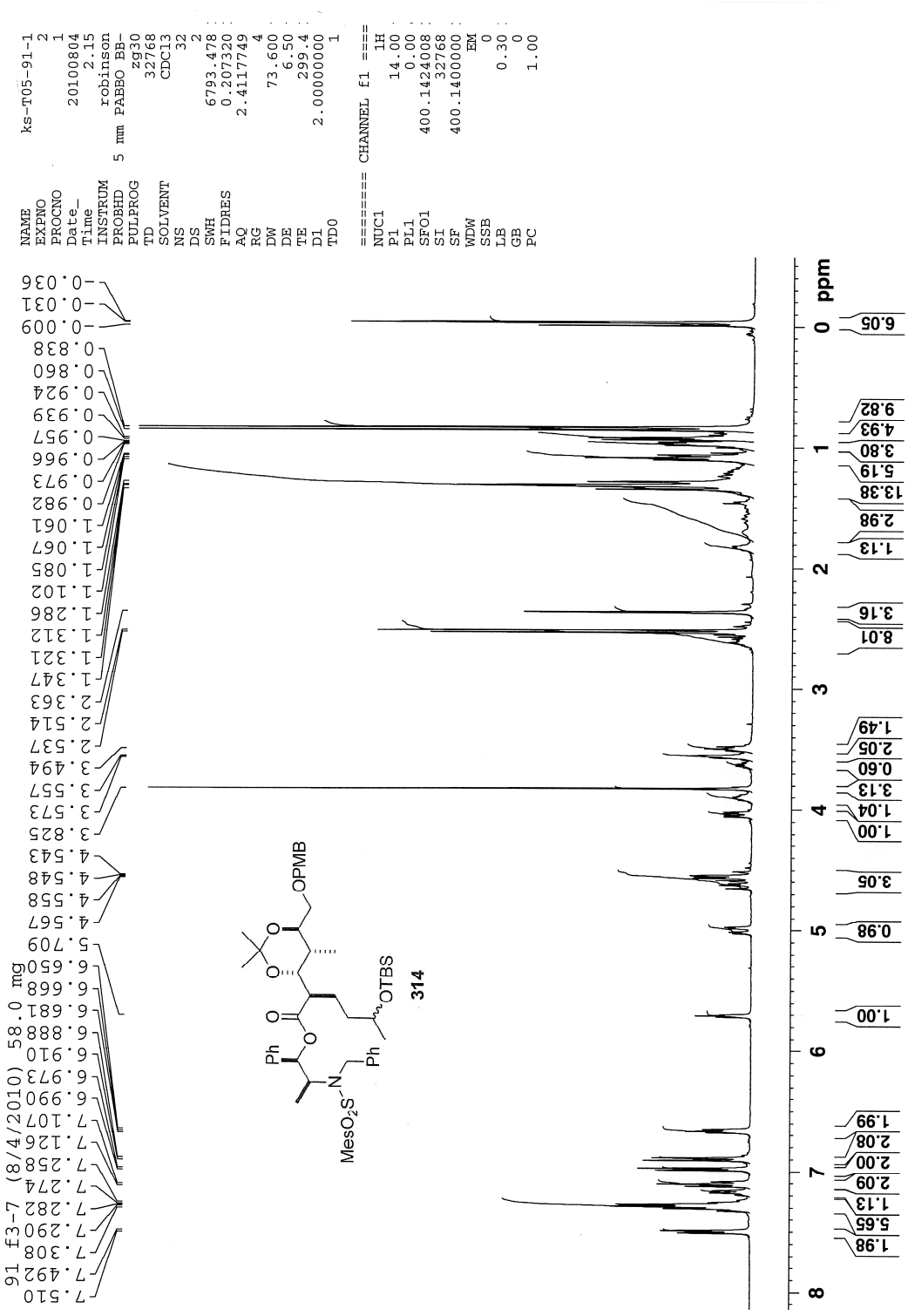

88 f9-24 (7/31/2010) 74.6 mg 13C
NAME ks-T05-88-1
EXPNO 8
PROCNO 1
Date_ 20100801
Time_ 17.29
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 18532
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 18390.4
DW 20.850 u
DE 6.50 u
TE 302.6 K
D1 0.20000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
SFO1 100.6253446 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
SFO2 400.1416006 M
SI 32768
SF 100.6152830 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
Ph
O
OH
OH
OPMB
O
N
Ph
MesO2S
OTBS
311
ppm

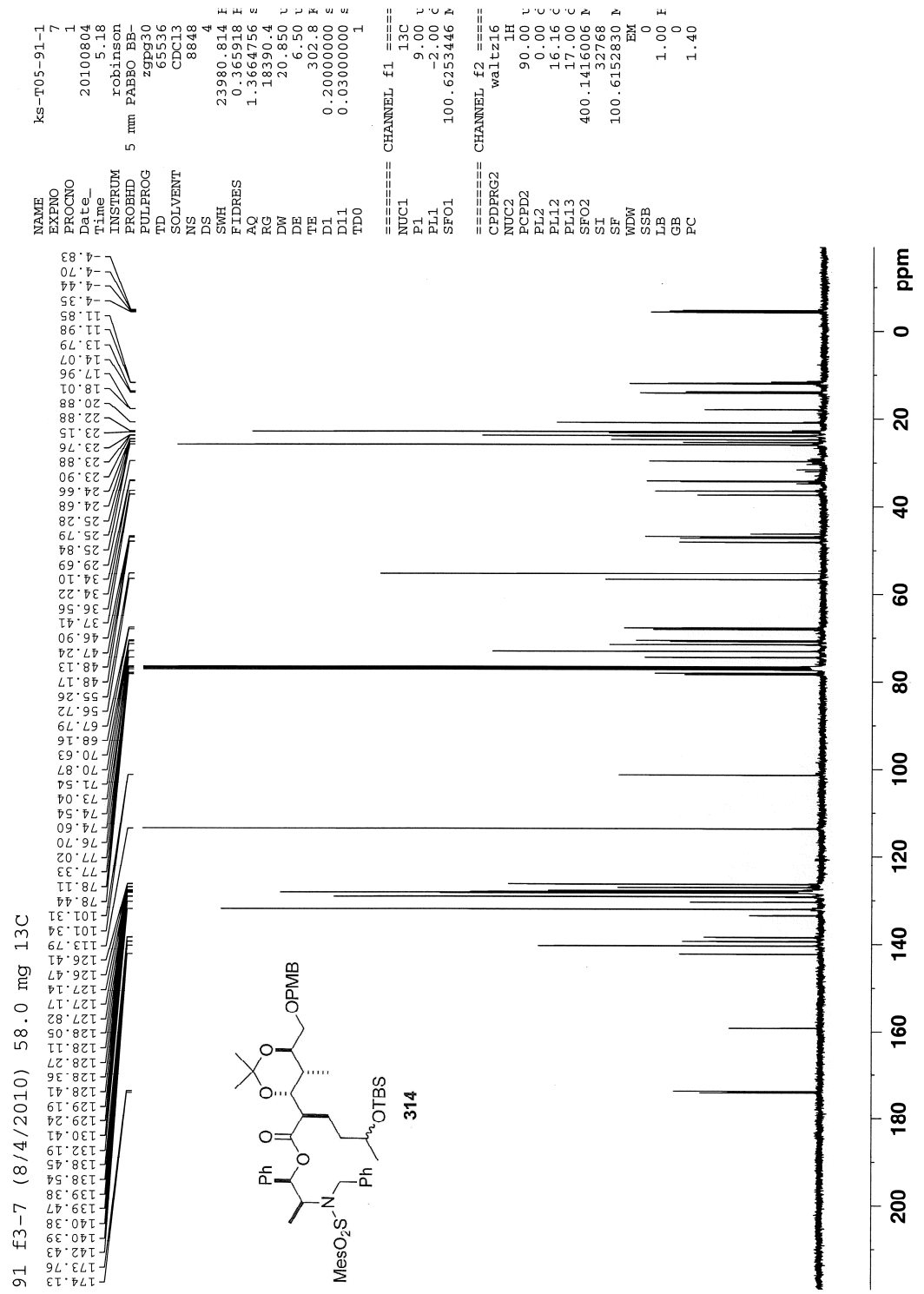

43 f28 (1/24/2011) 59.5 mg
312
Current Data Parameters
NAME ks-T08-43-1
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120124
Time_ 20.53
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 128
DW 78.000 use
DE 6.00 use
TE 296.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 15.00 use
PL1 -1.40 dB
SFO1 400.2628018 MHz
F2 - Processing parameters
SI 32768
SF 400.2600000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm

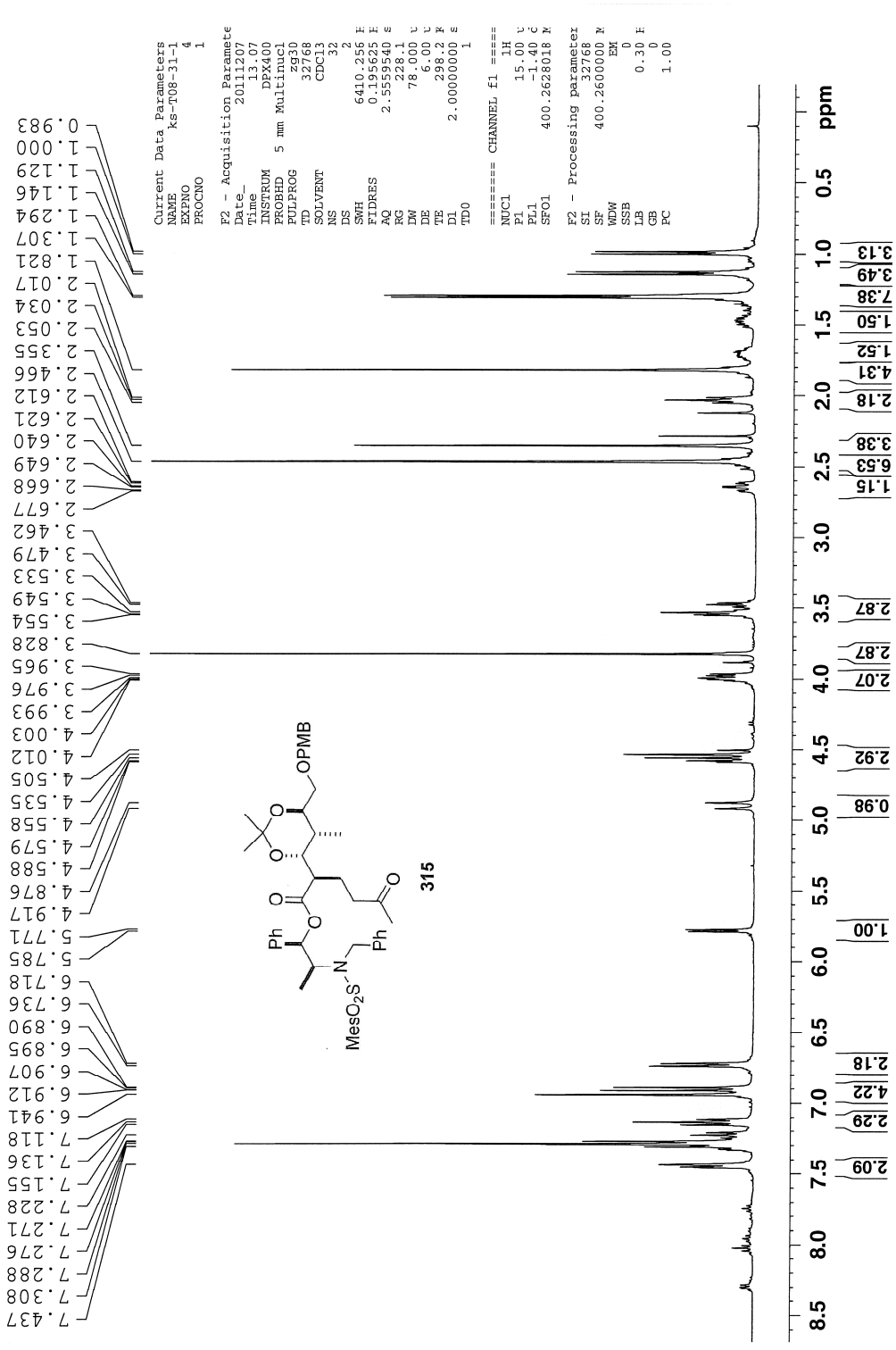

9 f4-15 (8/17/2010) 88.3 mg 13C
Current Data Parameters
NAME Ks-T06-09-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20100817
Time 23.04
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 15227
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3667775 sec
RG 7298.2
DW 20.850 usec
DE 6.00 usec
TE 300.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
174.78
174.57
159.41
142.51
140.43
138.32
132.14
129.78
129.46
128.28
128.19
128.00
127.09
126.69
126.63
113.92
78.16
77.40
77.08
76.76
73.71
73.14
72.23
67.27
56.57
55.28
48.12
35.71
29.70
23.45
23.39
22.91
20.90
14.20
14.05
9.69
Ph
O
OH
OH
OPMB
O
N
Ph
MesO2S
OH
312
ppm

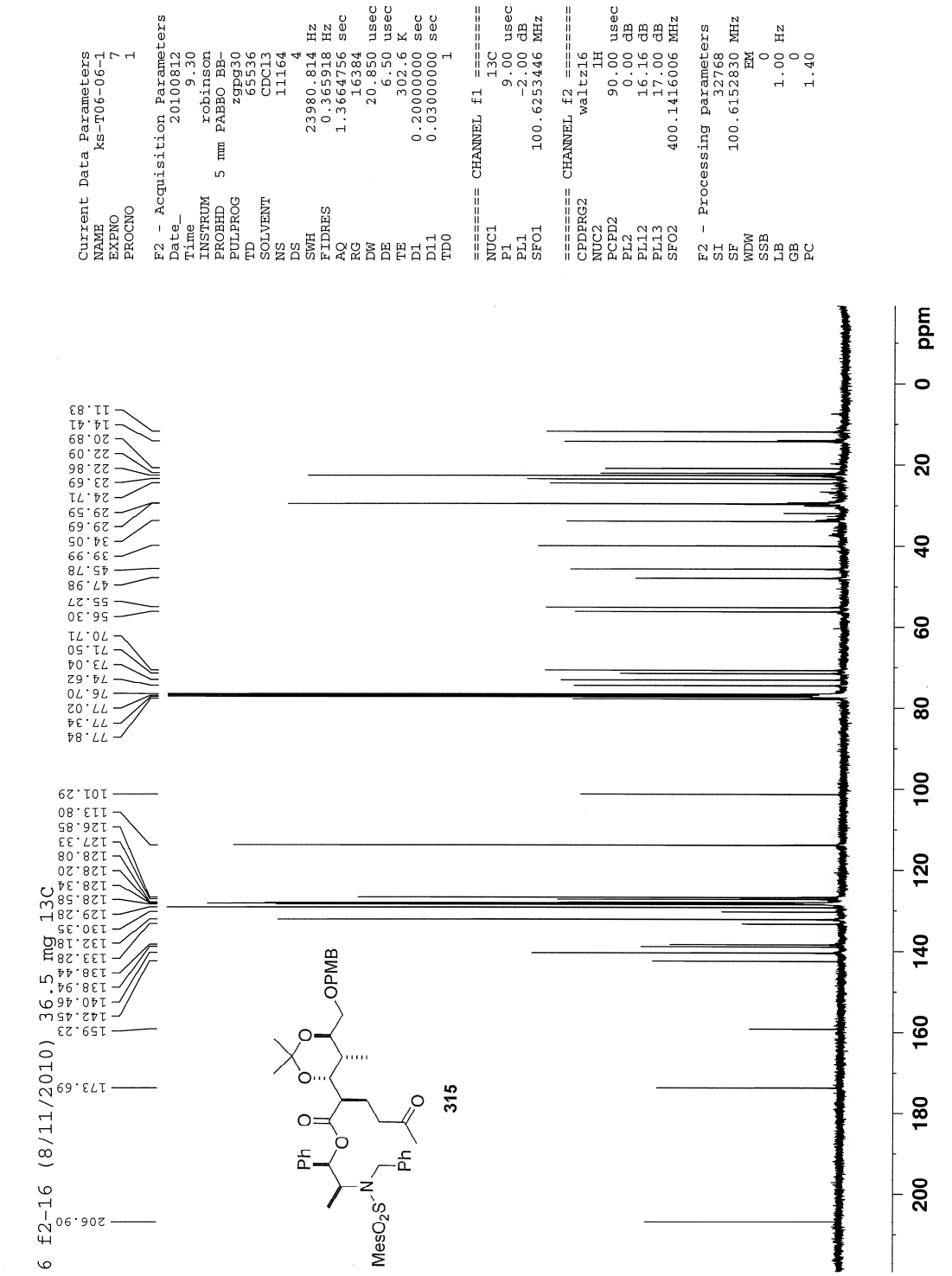

52 f9 (4/8/2012) 75.6 mg
313
OPMB
OH
Ph
Ph
MesO2S
ppm

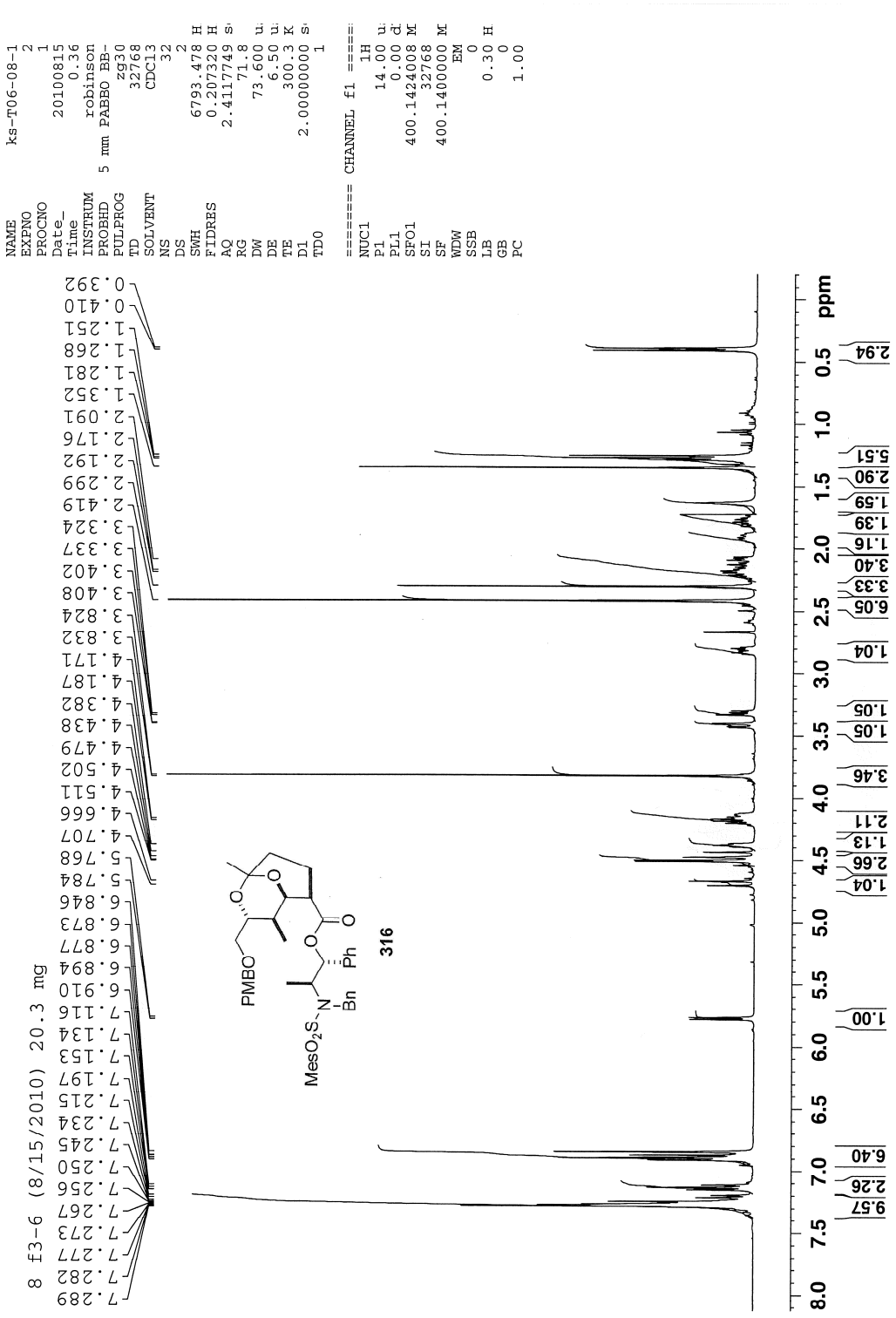

52 f9 (4/8/2012) 75.6 mg 13C
313
OPMB
Ph
Ph
MesO2S
OH
ppm

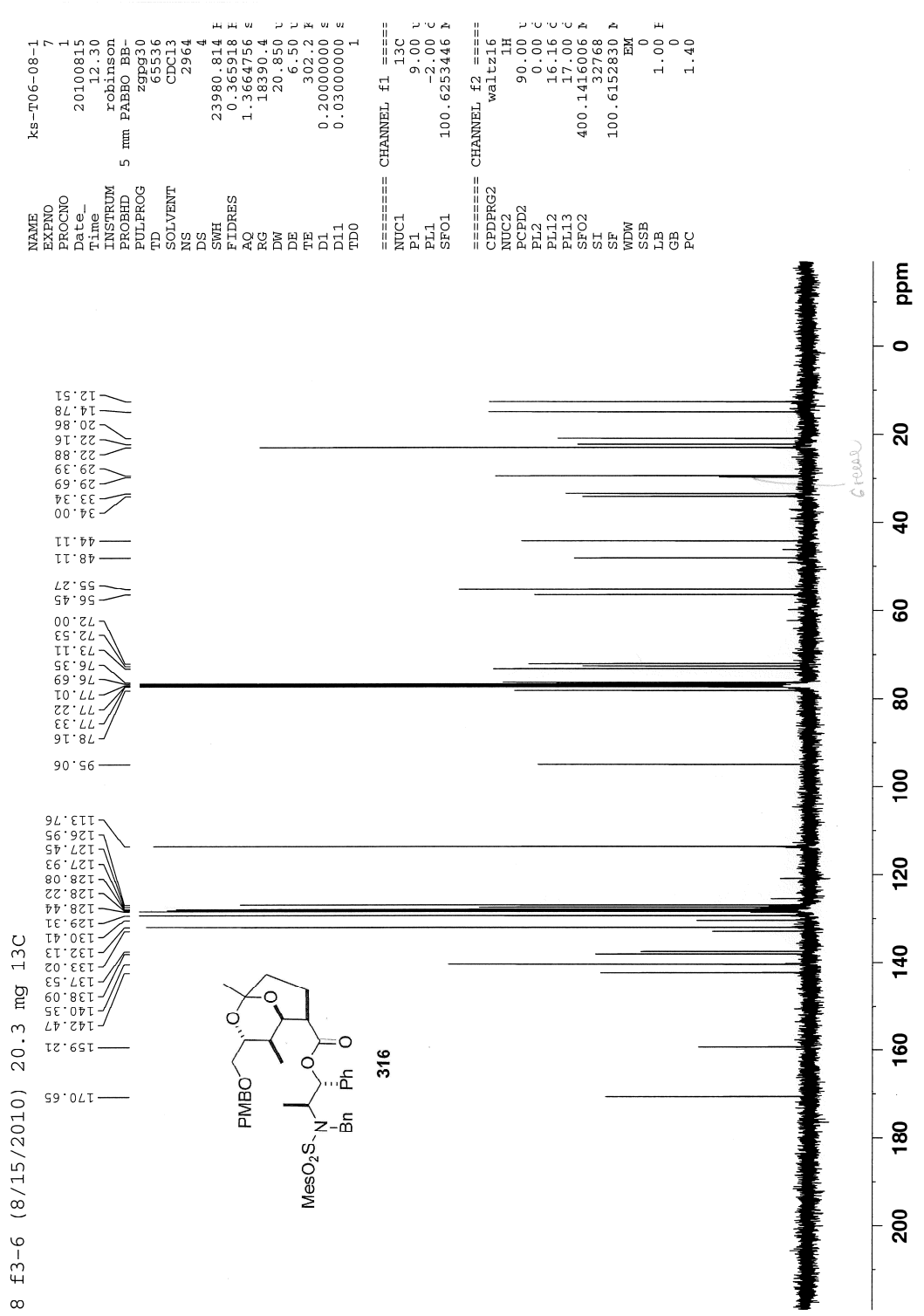

NAME ks-T05-91-1
EXPNO 2
PROCNO 1
Date_ 20100804
Time 2.15
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478
FIDRES 0.207320
AQ 2.4117749
RG 4
DW 73.600
DE 6.50
TE 299.4
D1 2.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 14.00
PL1 0.00
SFO1 400.1424008
SI 32768
SF 400.1400000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
91 f3-7 (8/4/2010) 58.0 mg
OPMB
OTBS
Ph
Ph
MesO2S
N
314
ppm

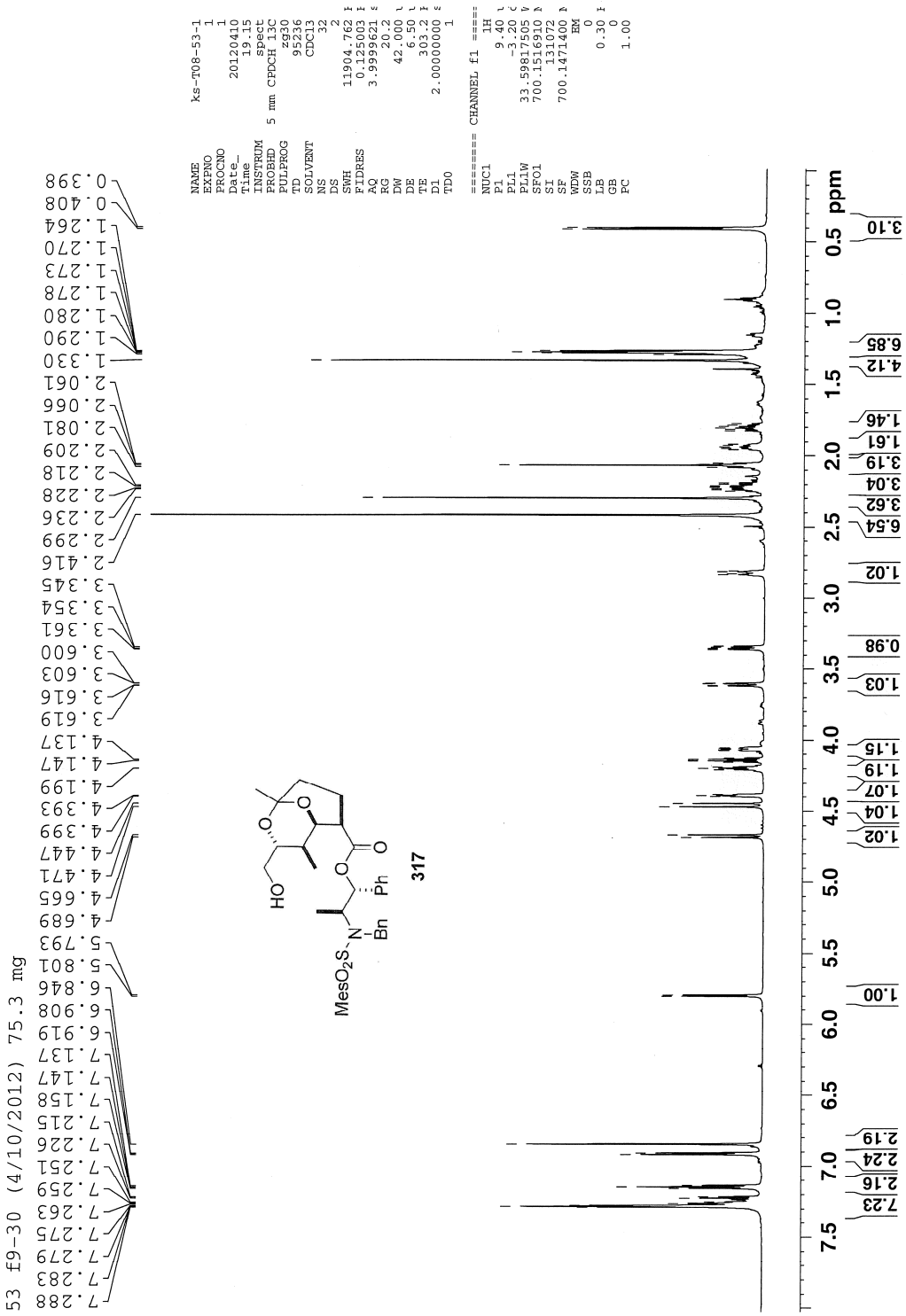

91 f3-7 (8/4/2010) 58.0 mg 13C
NAME ks-T05-91-1
EXPNO 7
PROCNO 1
Date_ 20100804
Time_ 5.18
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 8848
DS 4
SWH 23980.814
FIDRES 0.365918
AQ 1.3664756
RG 18390.4
DW 20.850
DE 6.50
TE 302.8
D1 0.20000000
D11 0.03000000
TD0 1
CHANNEL f1
NUC1 13C
P1 9.00
PL1 -2.00
SFO1 100.6253446
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00
PL2 0.00
PL12 16.16
PL13 17.00
SFO2 400.1416006
SI 32768
SF 100.6152830
WDW EM
SSB 0
LB 1.00
GB 0
PC 1.40
OPMB
OTBS
Ph
Ph
MesO2S
314
ppm


OPMB
Ph
Ph
N
MesO2S
315
ppm

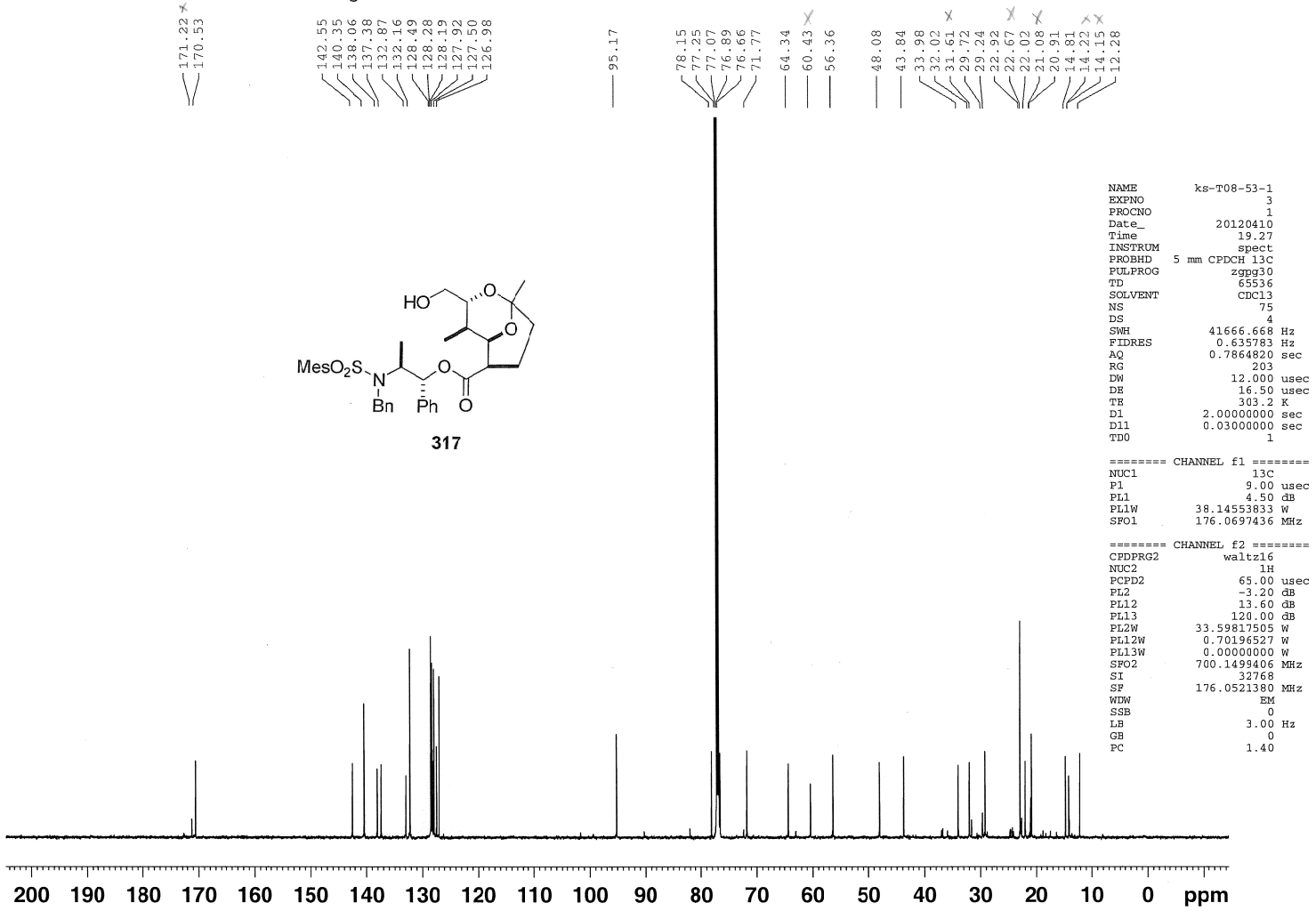

6 f2-16 (8/11/2010) 36.5 mg 13C
Current Data Parameters
NAME ks-T06-06-1
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100812
Time 9.30
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 11164
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 6.50 usec
TE 302.6 K
D1 0.20000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 -2.00 dB
SFO1 100.6253446 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 16.16 dB
PL13 17.00 dB
SFO2 400.1416006 MHz
F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
206.90
173.69
159.23
143.45
140.46
138.94
138.44
133.28
132.18
130.35
129.28
128.58
128.34
128.20
128.08
127.33
126.85
113.80
101.29
77.84
77.34
77.02
76.70
74.62
73.04
71.50
70.71
56.30
55.27
47.98
45.78
39.99
34.05
29.69
29.59
24.71
23.69
22.86
22.09
20.89
14.41
11.83
OPMB
Ph
Ph
MesO2S
N
315
200
180
160
140
120
100
80
60
40
20
0
ppm

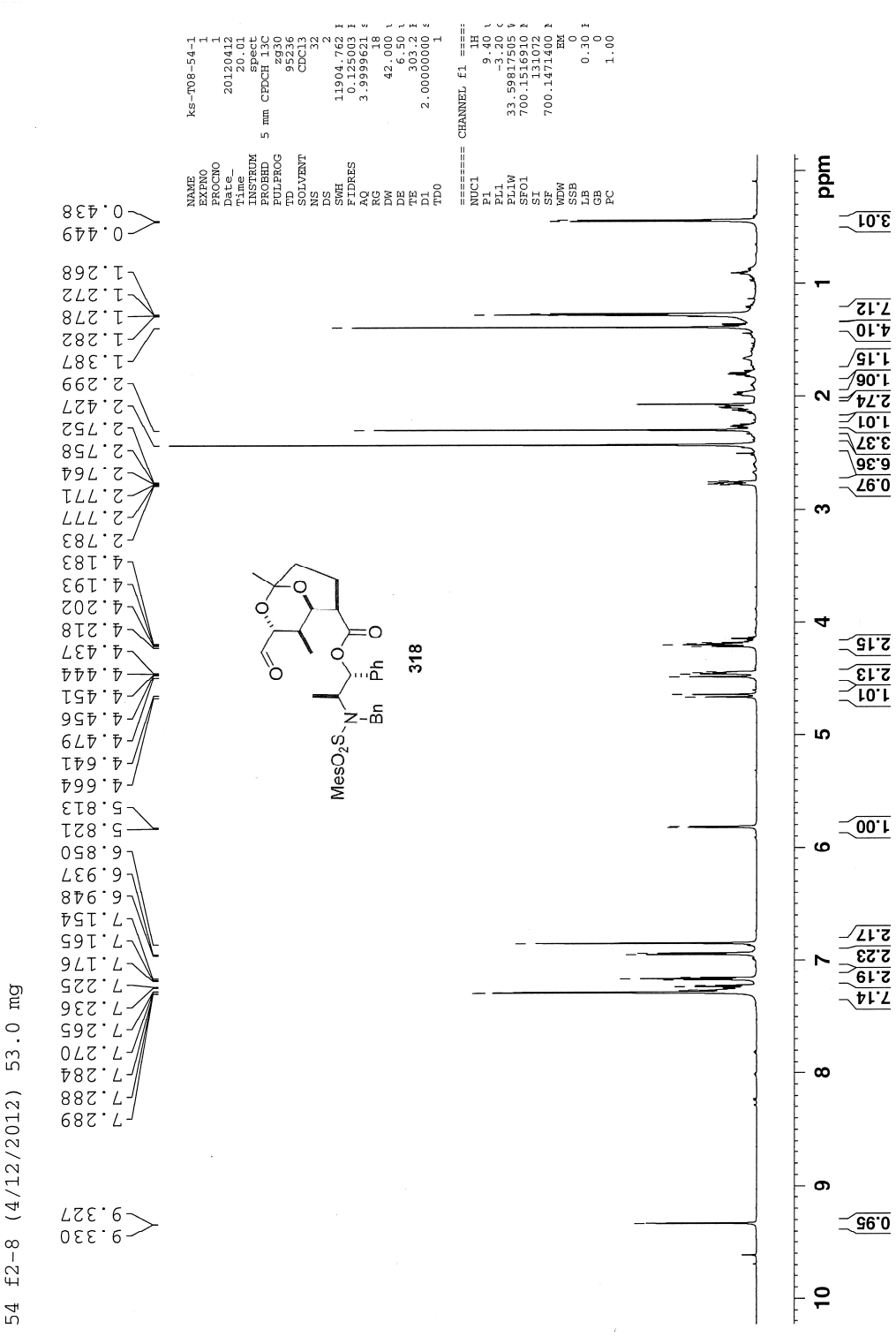

NAME ks-T06-08-1
EXPNO 2
PROCNO 1
Date_ 20100815
Time 0.36
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 71.8
DW 73.600 u
DE 6.50 u
TE 300.3 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
8 f3-6 (8/15/2010) 20.3 mg
316
PMBO
MesO2S
N
Bn
Ph
O
ppm

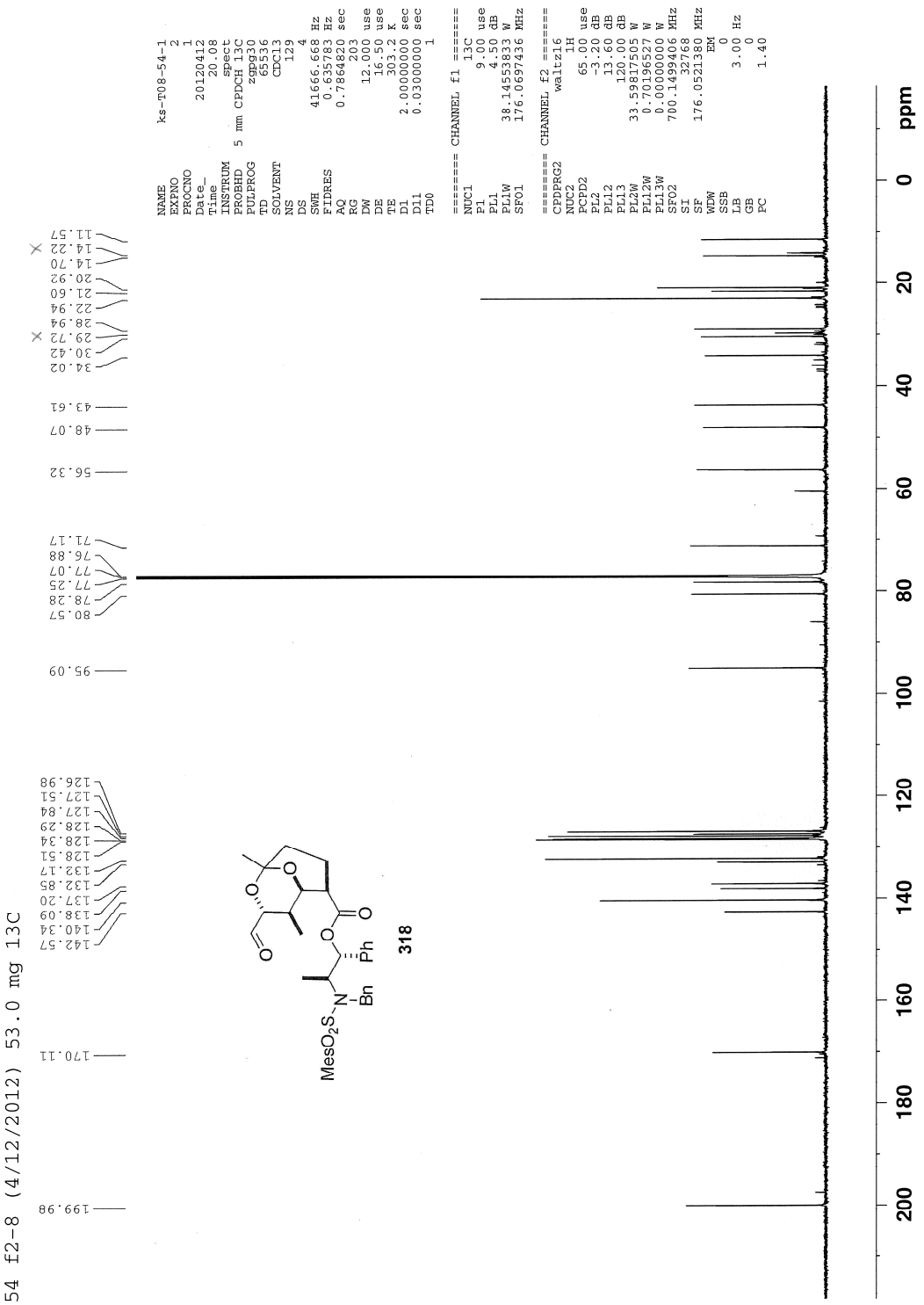

8 f3-6 (8/15/2010) 20.3 mg 13C
NAME ks-T06-08-1
EXPNO 7
PROCNO 1
Date_ 20100815
Time 12.30
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2964
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 18390.4
DW 20.850 u
DE 6.50 u
TE 302.2 K
D1 0.20000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
SFO1 100.6253446 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
SFO2 400.1416006 M
SI 32768
SF 100.6152830 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
170.65
159.21
142.47
140.35
138.09
137.53
133.02
132.13
130.41
129.31
128.44
128.22
128.08
127.93
127.45
126.95
113.76
95.06
78.16
77.33
77.22
77.01
76.69
76.35
73.11
72.53
72.00
56.45
55.27
48.11
44.11
34.00
33.34
29.69
29.39
22.88
22.16
20.86
14.78
12.51
PMBO
MesO2S
N
Bn
Ph
O
316
200
180
160
140
120
100
80
60
40
20
0
ppm

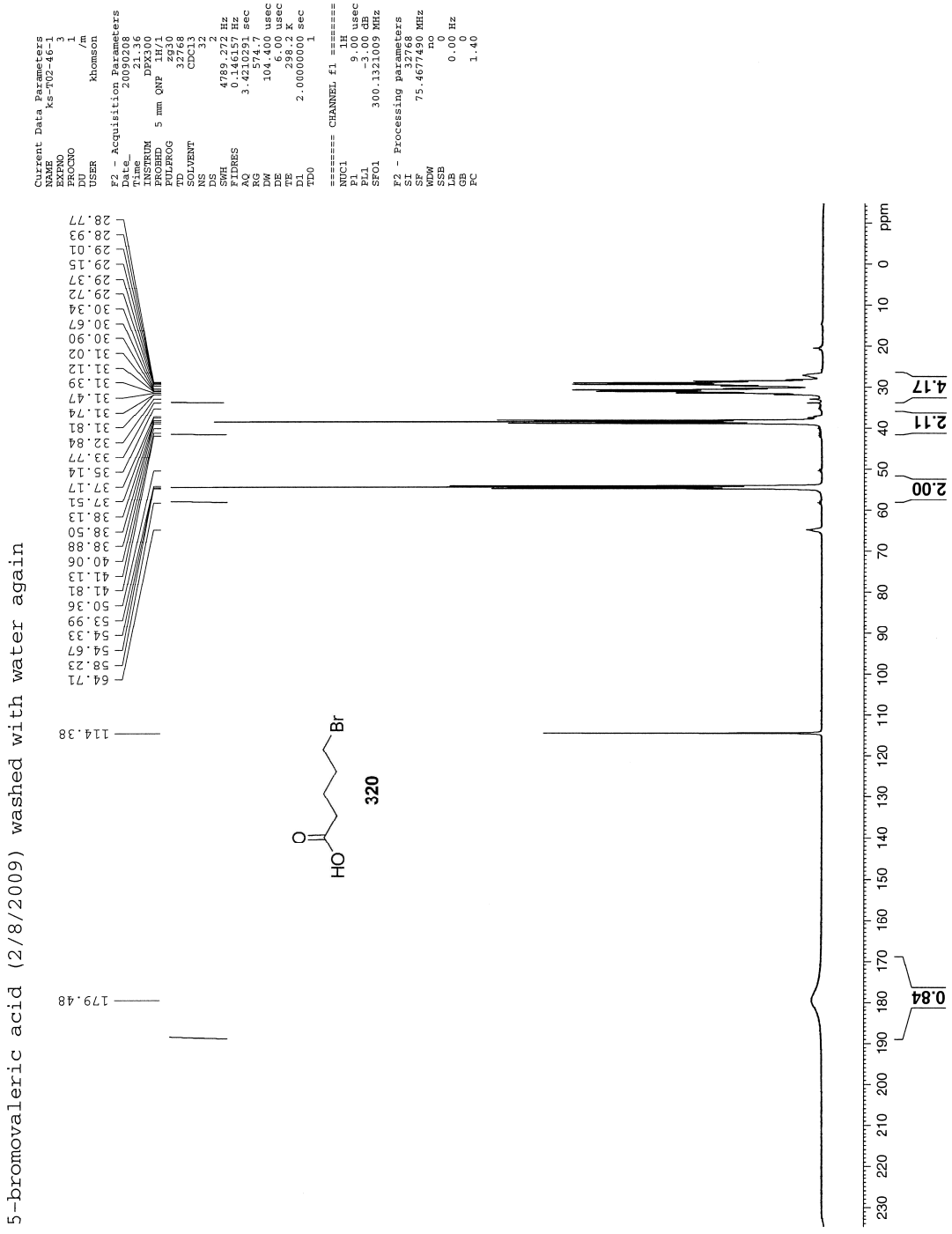

53 f9-30 (4/10/2012) 75.3 mg
317
MesO2S
N
Bn
Ph
HO
O
NAME ks-T08-53-1
EXPNO 1
PROCNO 1
Date_ 20120410
Time_ 19.15
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762
FIDRES 0.125003
AQ 3.9999621
RG 20.2
DW 42.000
DE 6.50
TE 303.2
D1 2.00000000
TD0 1
CHANNEL f1
NUC1 1H
P1 9.40
PL1 -3.20
PL1W 33.59817505
SFO1 700.1516910
SI 131072
SF 700.1471400
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
7.288
7.283
7.279
7.275
7.263
7.259
7.251
7.226
7.215
7.158
7.147
7.137
6.919
6.908
6.846
5.801
5.793
4.689
4.665
4.471
4.447
4.399
4.393
4.199
4.147
4.137
3.619
3.616
3.603
3.600
3.361
3.354
3.345
2.416
2.299
2.236
2.228
2.218
2.209
2.081
2.066
2.061
1.330
1.290
1.280
1.278
1.273
1.270
1.264
0.408
0.398
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5 ppm
7.23
2.16
2.24
2.19
1.00
1.02
1.04
1.07
1.19
1.15
0.98
1.03
1.02
3.10
6.54
3.62
3.04
3.19
1.61
1.46
6.85
4.12

53 f9-30 (4/10/2012) 75.3 mg 13C

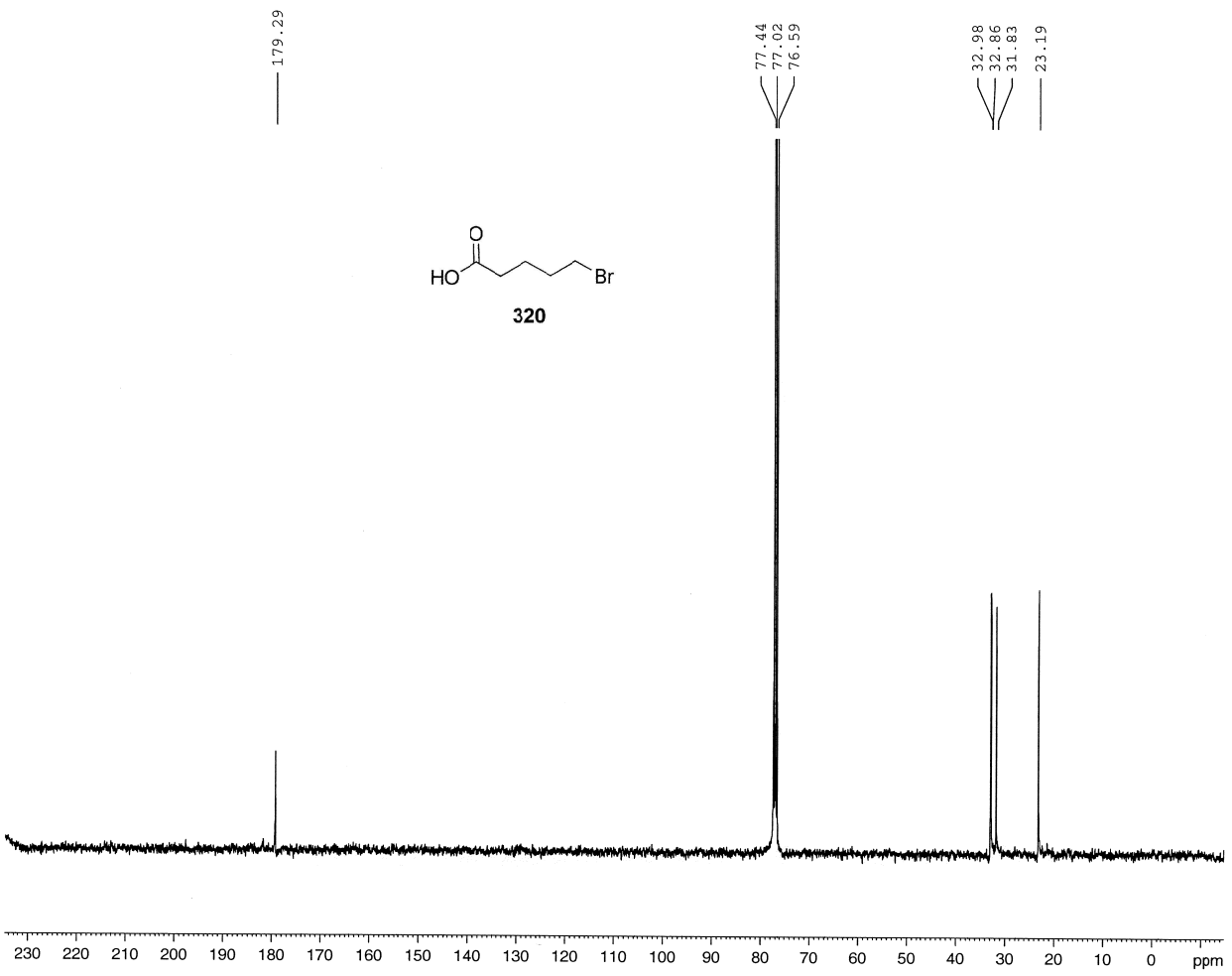



54 f2-8 (4/12/2012) 53.0 mg
318
MesO2S
Bn
Ph
ppm

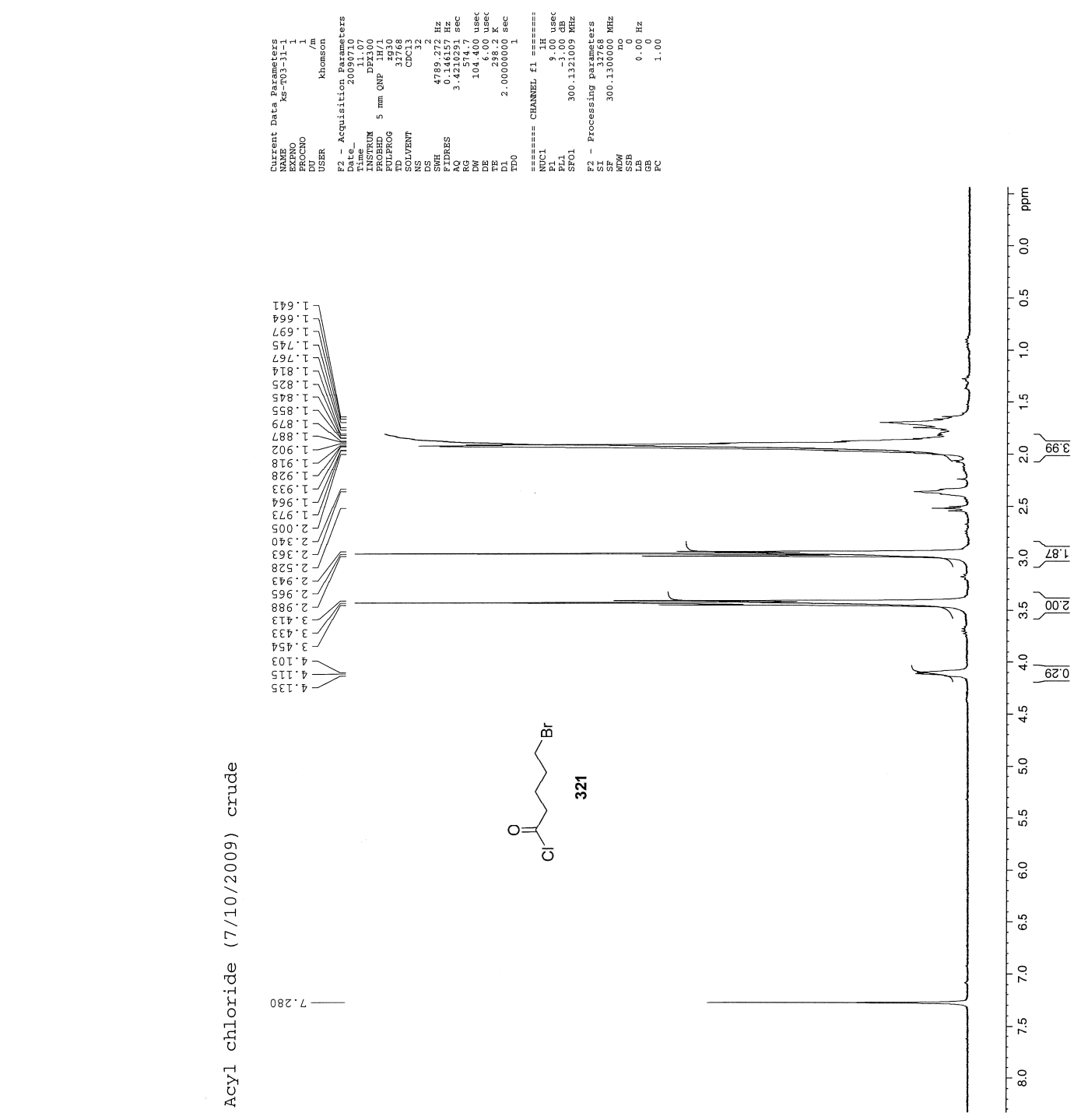

54 f2-8 (4/12/2012) 53.0 mg 13C
199.98
170.11
142.57
140.34
138.09
137.20
132.85
132.17
128.51
128.34
128.29
127.84
127.51
126.98
95.09
80.57
78.28
77.25
77.07
76.88
71.17
56.32
48.07
43.61
34.02
30.42
29.72
28.94
22.94
21.60
20.92
14.70
14.22
11.57
NAME ks-T08-54-1
EXPNO 2
PROCNO 1
Date_ 20120412
Time 20.08
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 129
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 use
DE 16.50 use
TE 303.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 =======
NUC1 13C
P1 9.00 use
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 use
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
MesO2S
N
Bn
Ph
O
318
200
180
160
140
120
100
80
60
40
20
0
ppm

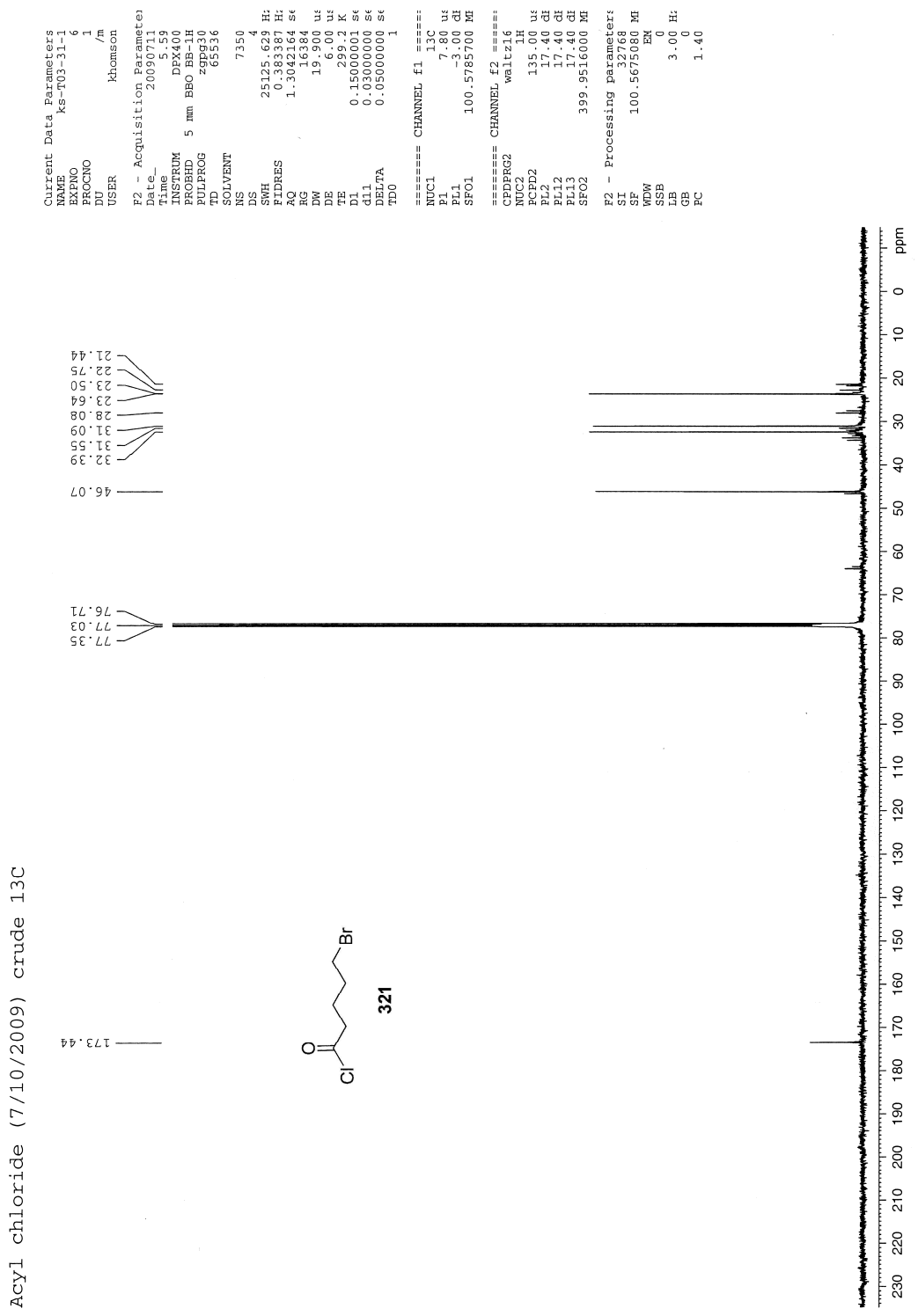

5-bromovaleric acid (2/8/2009) washed with water again
Current Data Parameters
NAME ks-702-46-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090208
Time 21.36
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
64.71
58.23
54.67
54.33
53.99
50.36
41.81
41.13
40.06
38.88
38.50
38.13
37.51
37.17
35.14
33.77
32.84
31.81
31.74
31.47
31.39
31.12
31.02
30.90
30.67
30.34
29.72
29.37
29.15
29.01
28.93
28.77
114.38
179.48
Br
O
HO
320
4.17
2.11
2.00
0.84
ppm

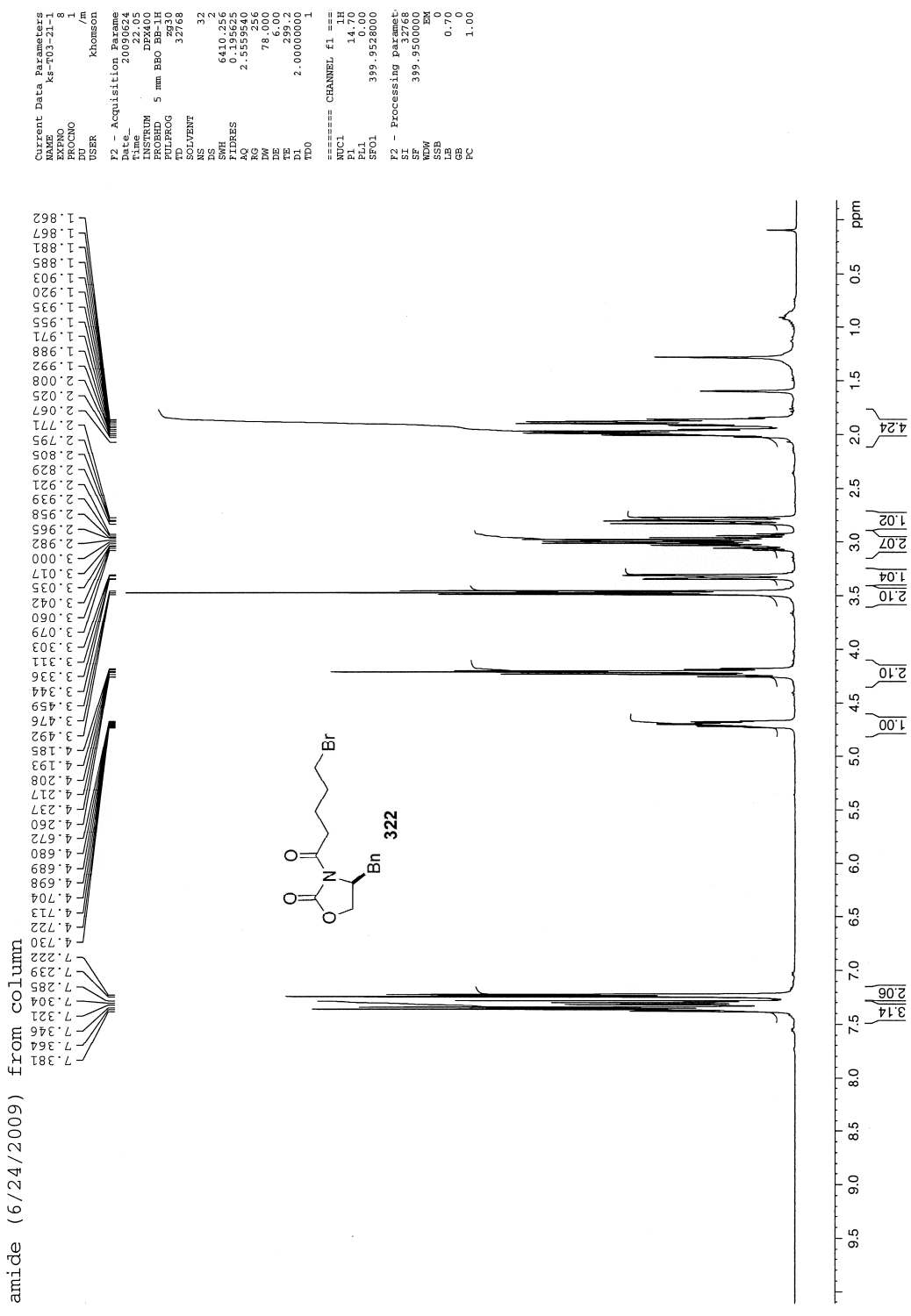
5-bromovaleric acid (2/8/2009) washed with water again

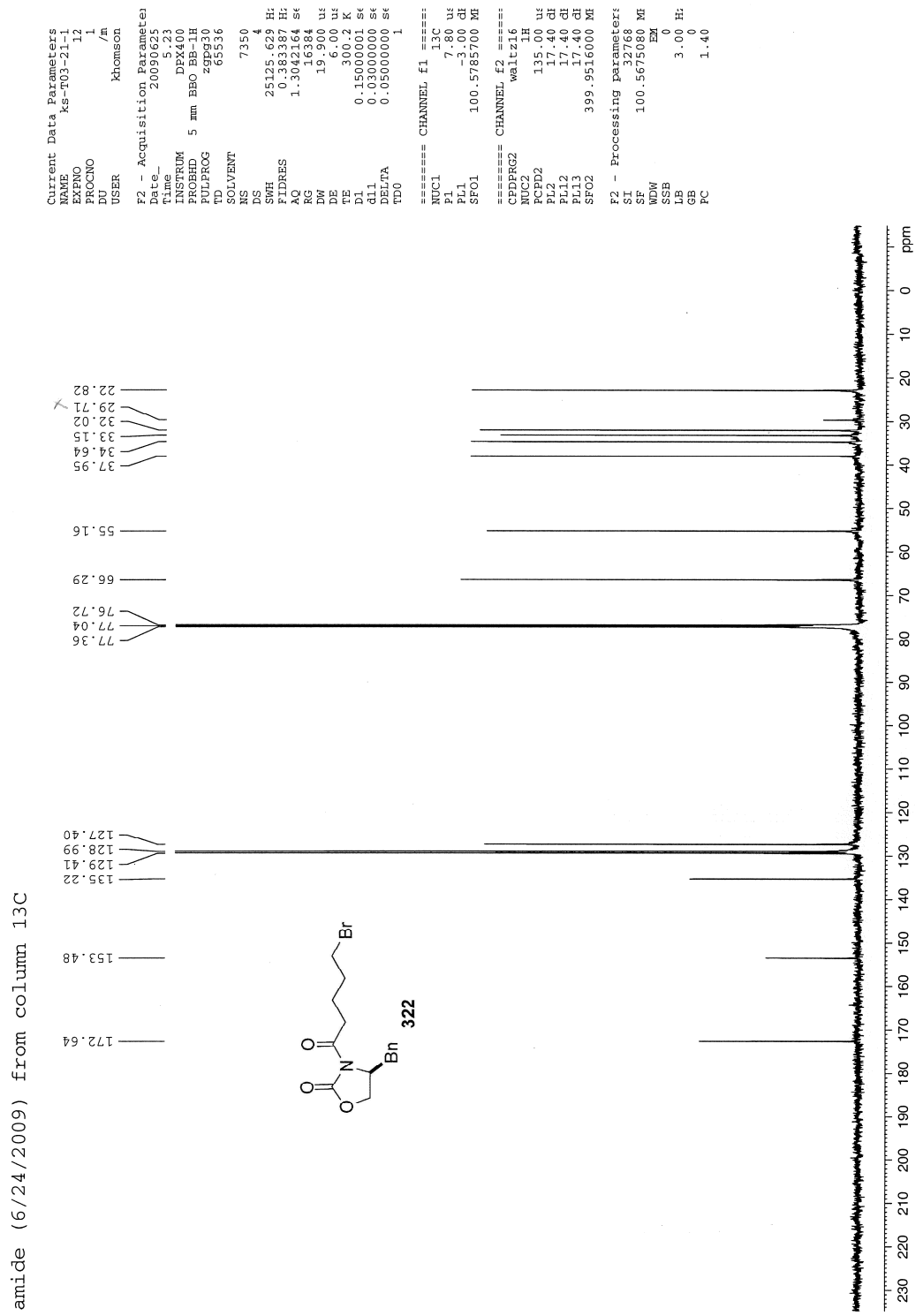


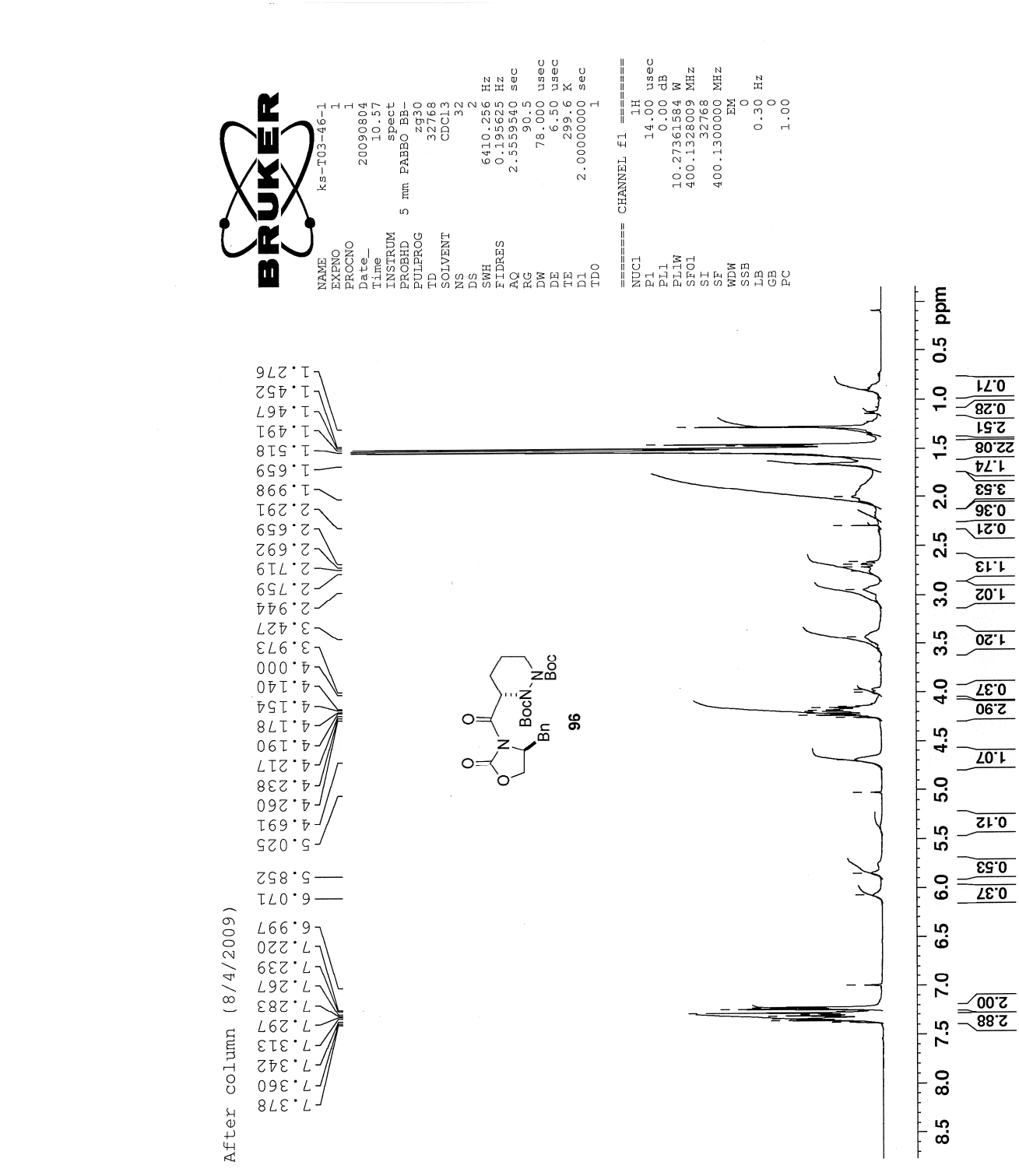

```
Current Data Parameters
NAME         ks-T02-46-1
EXPNO                  4
PROCNO                 1
DU                    /m
USER             khomson

F2 - Acquisition Parameter
Date_           20090208
Time               22.40
INSTRUM          DPX300
PROBHD   5 mm QNP  1H/1
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1850
DS                    4
SWH           18832.393 Hz
FIDRES         0.287360 Hz
AQ             1.7400308 se
RG                9195.2
DW                26.550 us
DE                 6.00 us
TE                298.2 K
D1           0.15000001 se
d11          0.03000000 se
DELTA        0.05000000 se
TD0                    1

======== CHANNEL f1 ======
NUC1                13C
P1                 8.80 us
PL1               -3.00 dB
SFO1         75.4760505 MH

======== CHANNEL f2 ======
CPDPRG2         waltz16
NUC2                1H
PCPD2            80.00 us
PL2              -3.00 dB
PL12             17.55 dB
PL13             17.55 dB
SFO2        300.1312005 MH

F2 - Processing parameters
SI                 32768
SF          75.4677490 MH
WDW                   EM
SSB                    0
LB                 3.00 Hz
GB                     0
PC                  1.40
```


Acyl chloride (7/10/2009) crude
Current Data Parameters
NAME Ks-703-31-1
EXPNO 1
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090710
Time 11.07
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146151 Hz
AQ 3.4210751 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW 0
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.280
4.135
4.115
4.103
3.454
3.433
3.413
2.988
2.965
2.943
2.528
2.363
2.340
2.005
1.973
1.964
1.933
1.928
1.918
1.902
1.887
1.879
1.855
1.845
1.825
1.814
1.767
1.745
1.697
1.664
1.641
Br
O
Cl
321
3.99
1.87
2.00
0.29
ppm

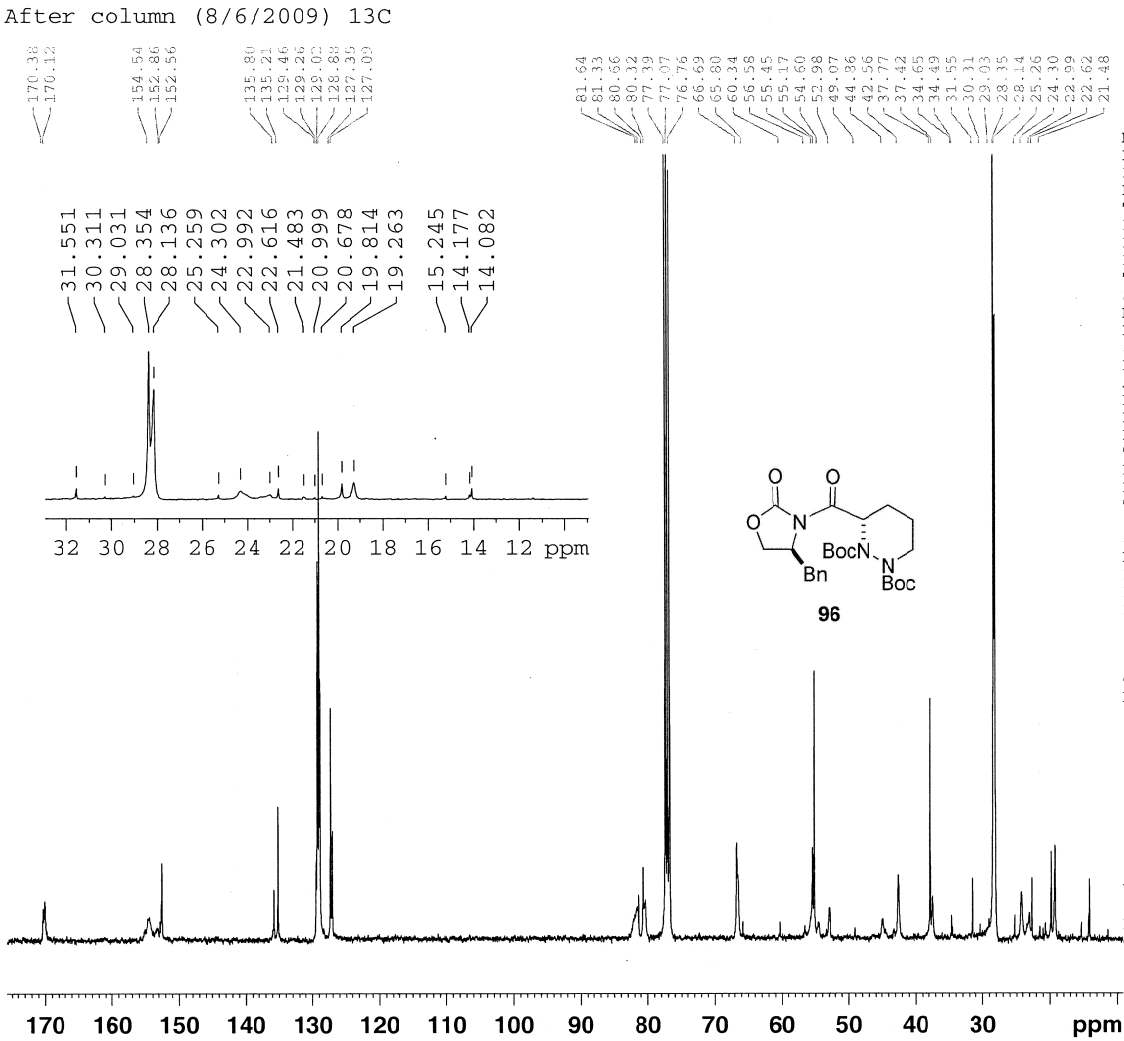

Acyl chloride (7/10/2009) crude 13C
Current Data Parameters
NAME ks-T03-31-1
EXPNO 6
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20090711
Time 5.59
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 7350
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 299.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
173.44
77.35
77.03
76.71
46.07
32.39
31.55
31.09
28.08
23.64
23.50
22.75
21.44
O
Cl
Br
321
ppm


amide (6/24/2009) from column
Current Data Parameters
NAME ks-T03-2i-1
EXPNO 8
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parame
Date_ 20090624
Time 22.05
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 256
DW 78.000
DE 6.00
TE 299.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing paramet
SI 32768
SF 399.9500000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
322
Br
Bn
O
N
O
O
4.24
2.07
1.02
2.10
1.04
2.10
1.00
3.14
2.06
ppm


amide (6/24/2009) from column 13C
Current Data Parameters
NAME ks-T03-21-1
EXPNO 12
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20090625
Time 5:23
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 7350
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.30442164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 300.2 K
D1 0.15000001 s
dl1 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
22.82
29.71
32.02
33.15
34.64
37.95
55.16
66.29
76.72
77.04
77.36
127.40
128.99
129.41
135.22
153.48
172.64
Br
O
N
O
O
Bn
322
ppm


After column (8/4/2009)
BRUKER
NAME ks-T03-46-1
EXPNO 1
PROCNO 1
Date_ 20090804
Time 10.57
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 90.5
DW 78.000 usec
DE 6.50 usec
TE 299.6 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1328009 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
BocN
Boc
Bn
96
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.88 2.00 0.37 0.53 0.12 1.07 2.90 0.37 1.20 1.02 1.13 0.21 0.36 3.53 1.74 22.08 2.51 0.28 0.71

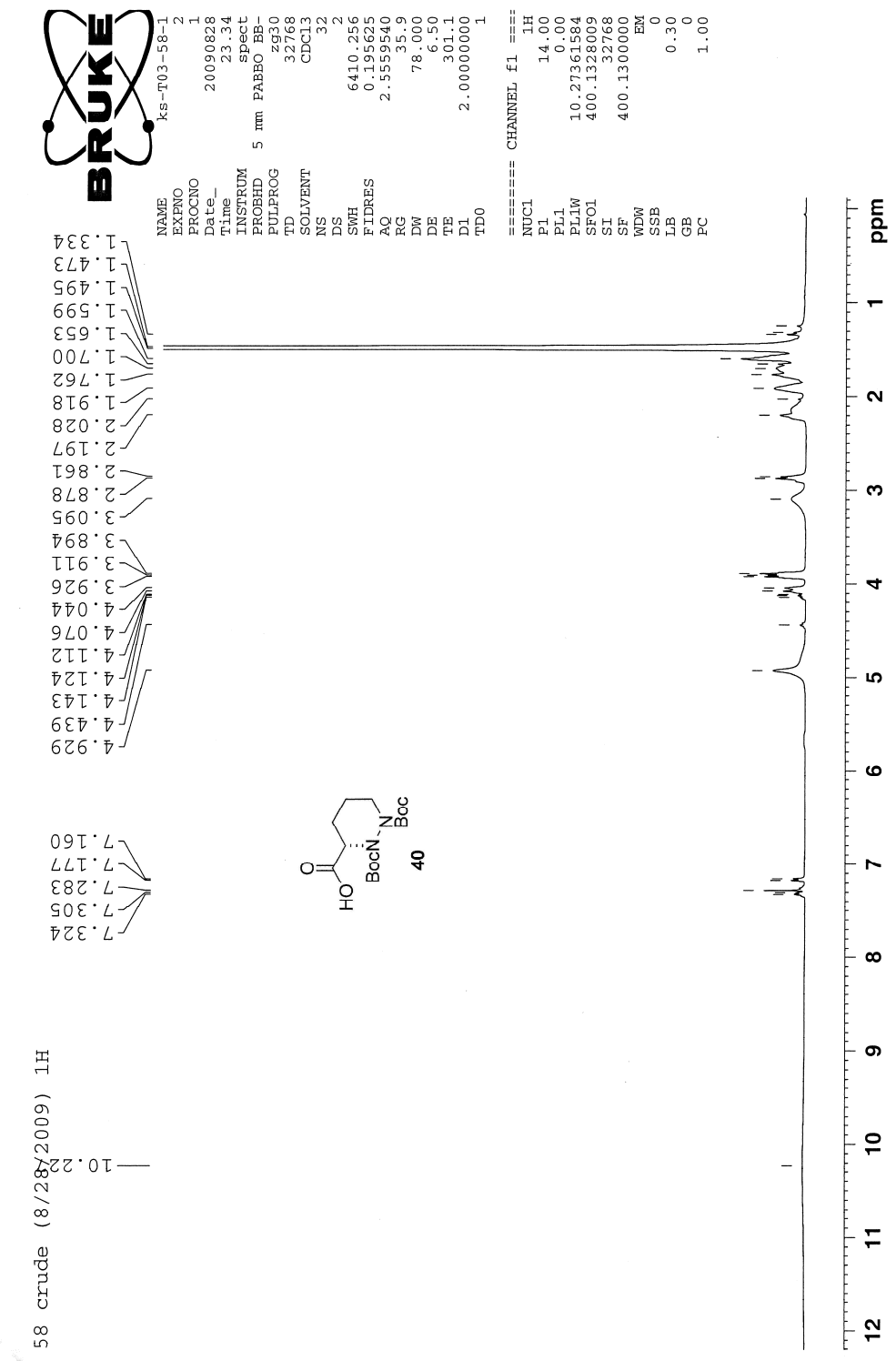
After column (8/6/2009) 13C



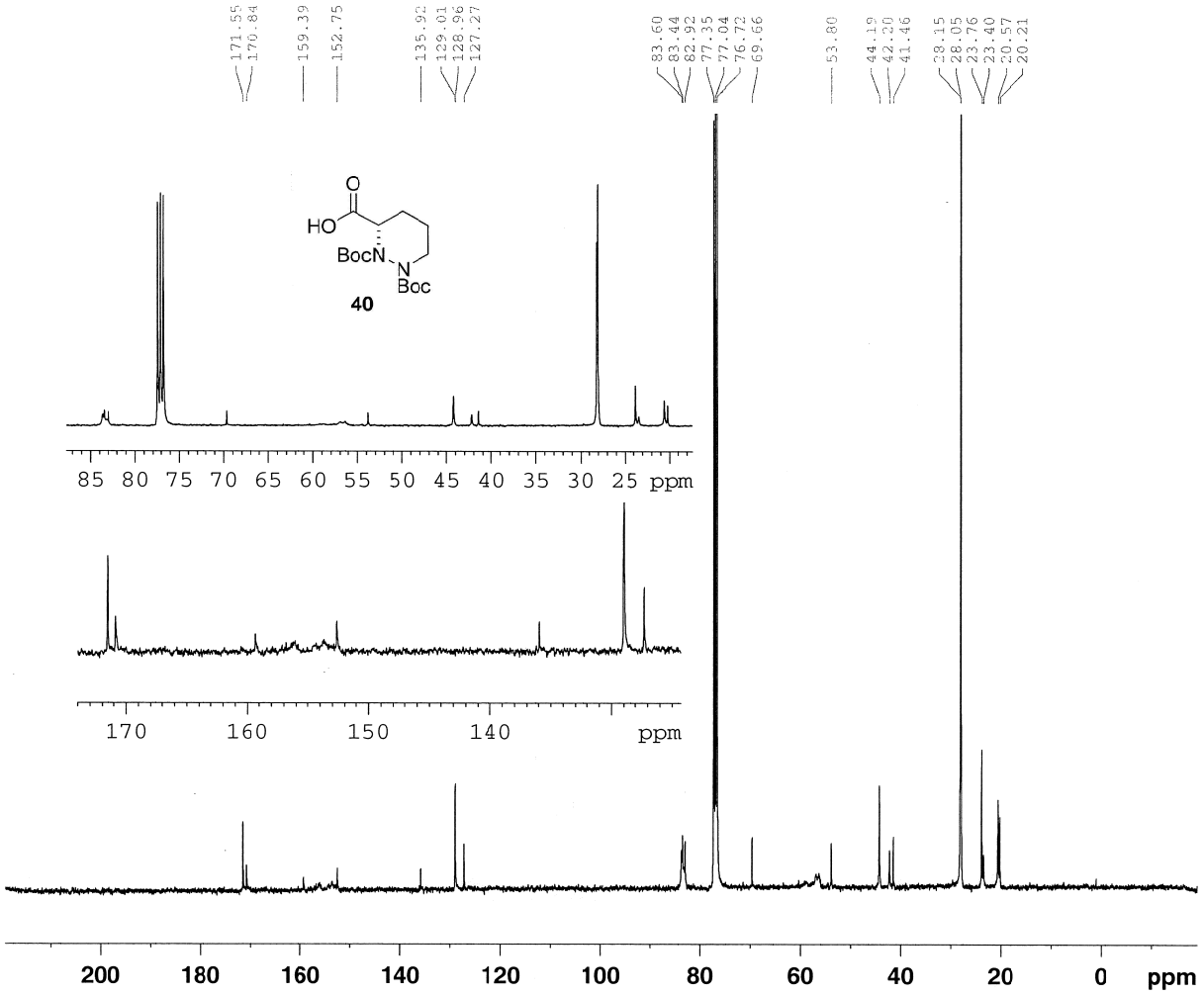
96

BRUKER

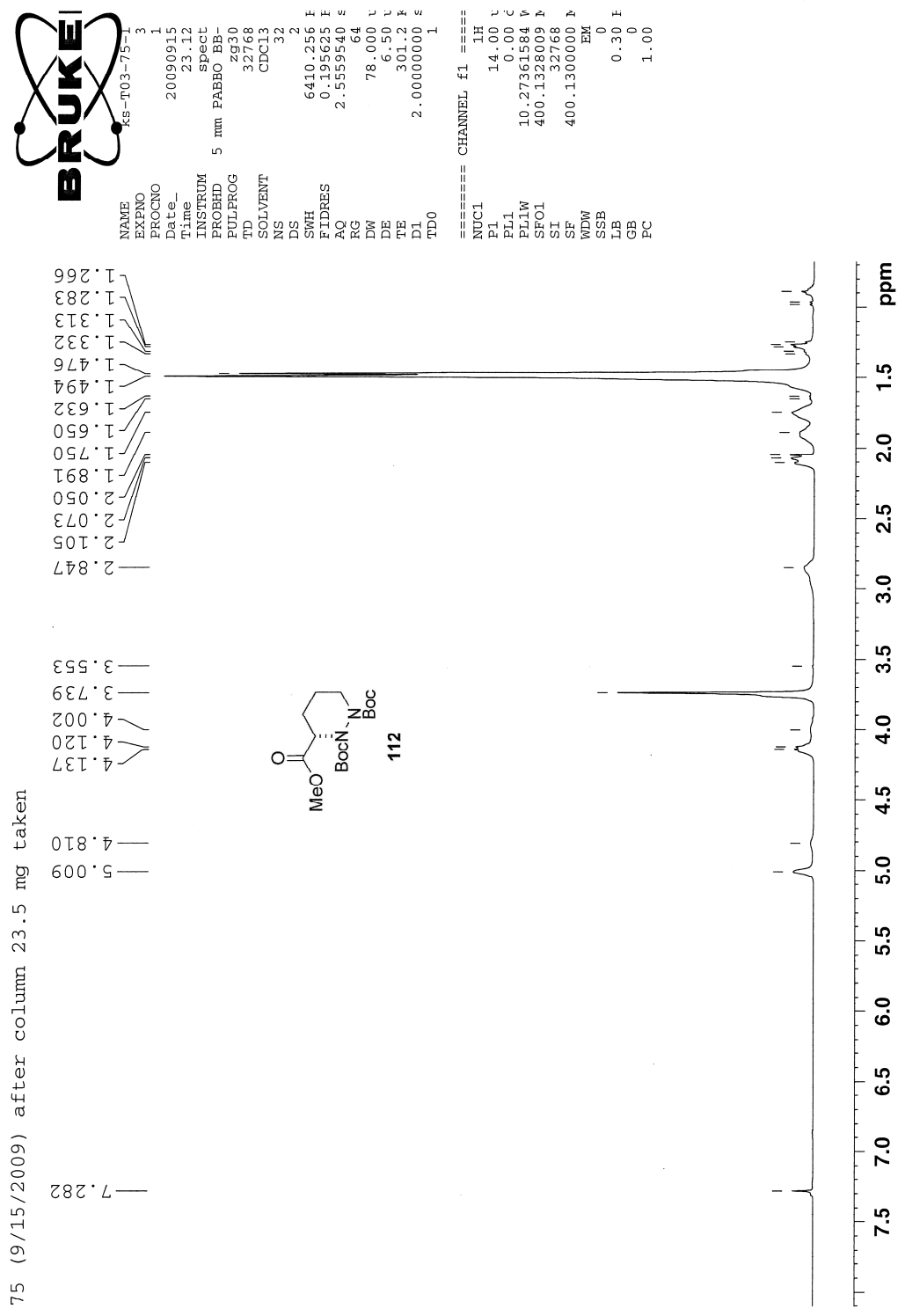
NAME	ks-T03-47-1
EXPNO	5
PROCNO	1
Date_	20090807
Time	7.28
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3072
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	18390.4
DW	20.850 usec
DE	6.50 usec
TE	300.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	-2.00 dB
PL1W	46.89702606 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
PL2W	10.27361584 W
PL12W	0.24872722 W
PL13W	0.20498557 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127690 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

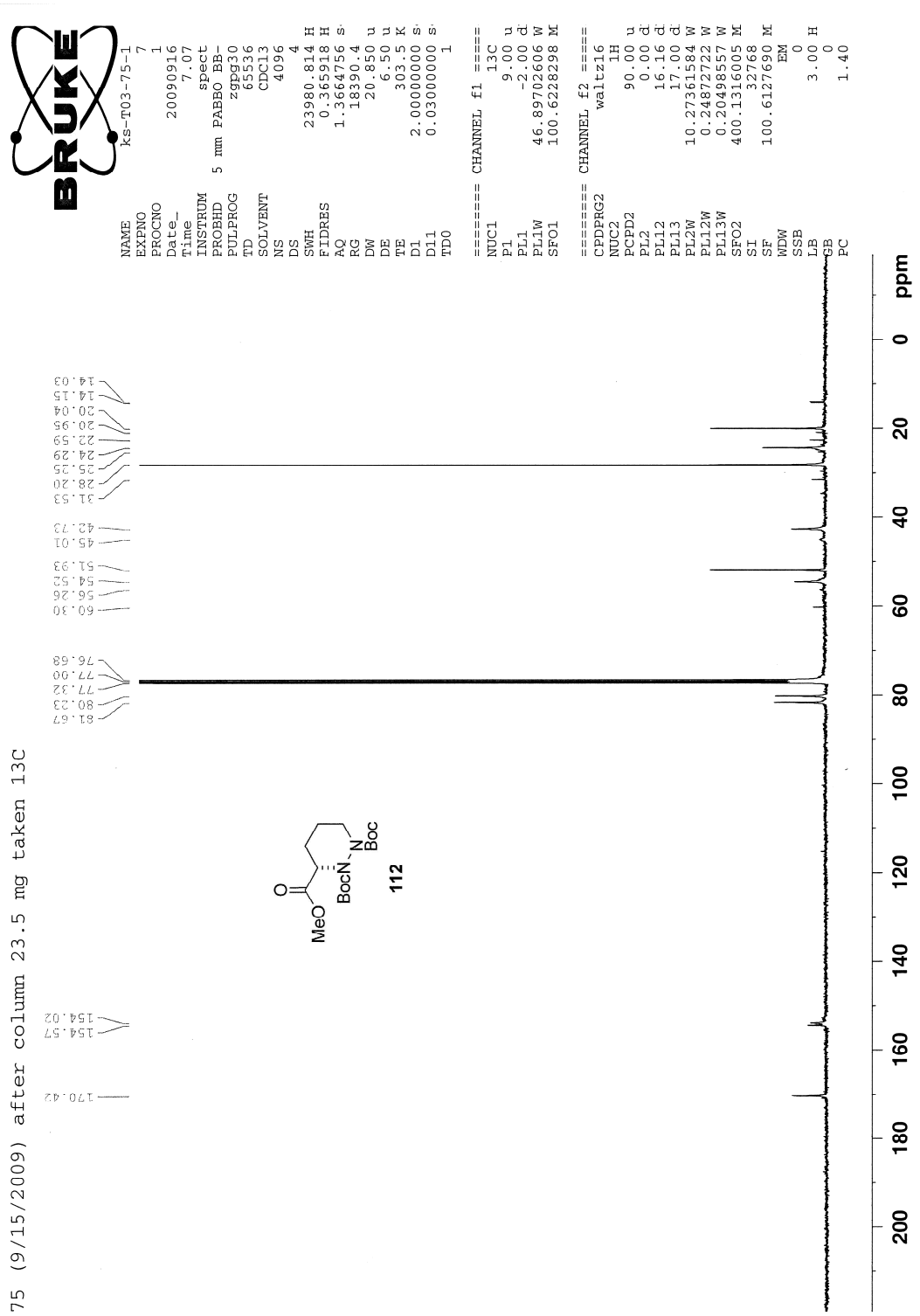

58 crude (8/28/2009) 1H
ks-T03-58-1
NAME 2
EXPNO 2
PROCNO 1
Date_ 20090828
Time 23.34
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 35.9
DW 78.000
DE 6.50
TE 301.1
D1 2.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 14.00
PL1 0.00
PL1W 10.27361584
SFO1 400.1328009
SI 32768
SF 400.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
10.22
7.324
7.305
7.283
7.177
7.160
4.929
4.439
4.143
4.124
4.112
4.076
4.044
3.926
3.911
3.894
3.095
2.878
2.861
2.197
2.028
1.918
1.762
1.700
1.653
1.599
1.495
1.473
1.334
HO
O
BocN
N
Boc
40
12
11
10
9
8
7
6
5
4
3
2
1
ppm

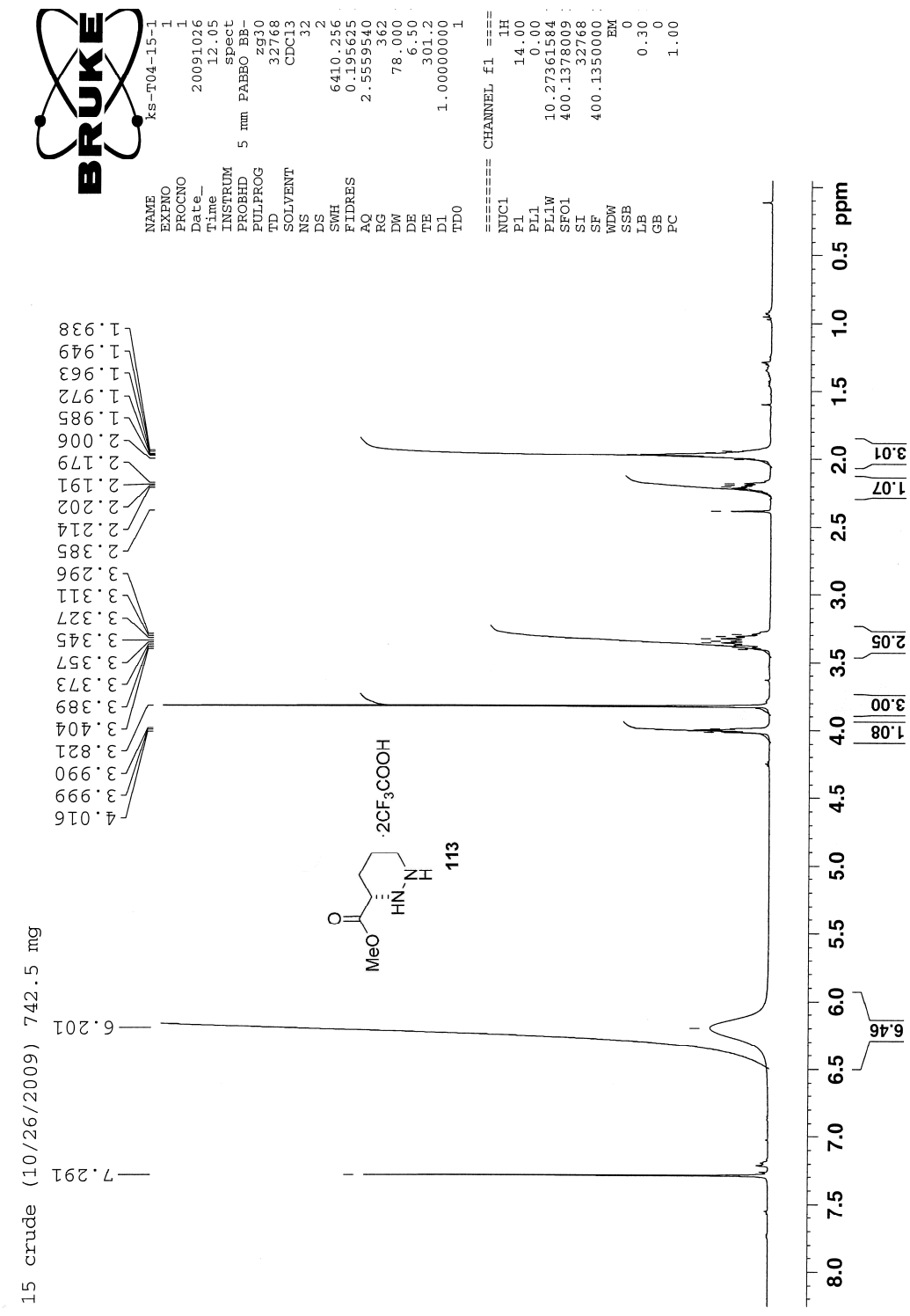
Hydrolysis (8/16/2009) white solid product 13C

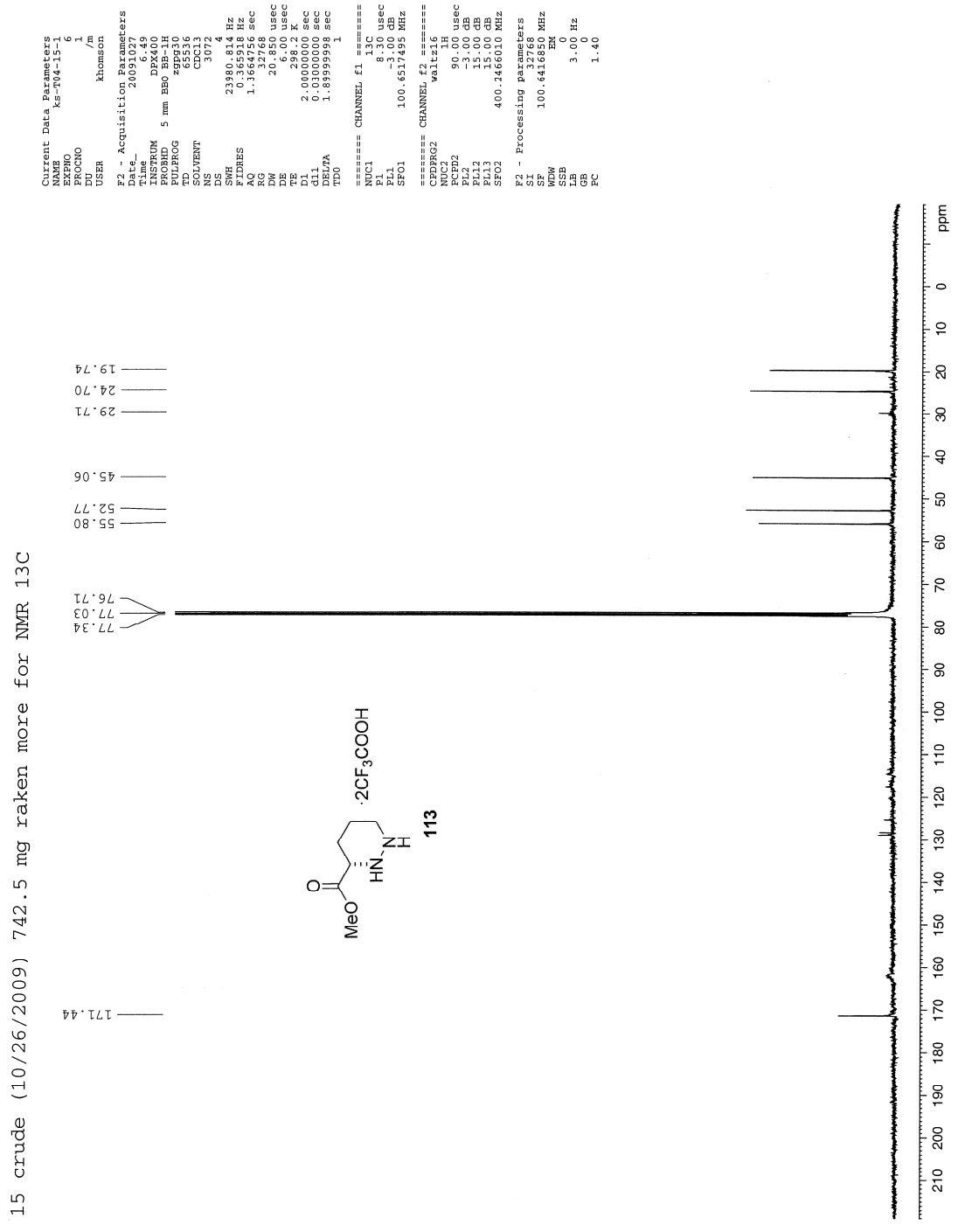


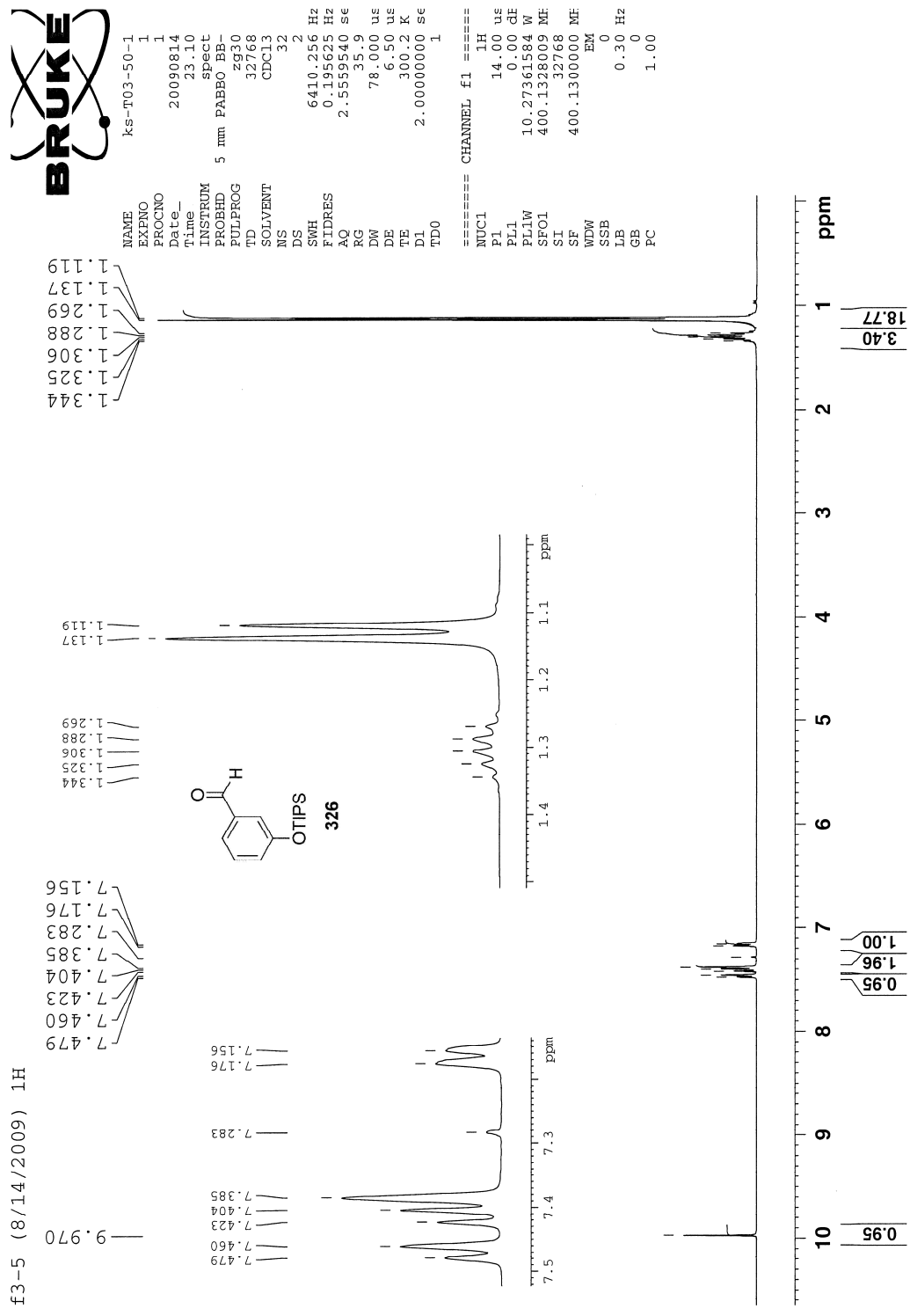
NAME	ks-T03-54-1
EXPNO	5
PROCNO	1
Date_	20090817
Time	7.27
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3584
DS	4
SWH	23980.814
FIDRES	0.365918
AQ	1.3664756
RG	18390.4
DW	20.850
DE	6.50
TE	301.2
D1	2.00000000
D11	0.03000000
TD0	1
======== CHANNEL f1 ====	
NUC1	13C
P1	9.00
PL1	-2.00
PL1W	46.89702606
SFO1	100.6228298
======== CHANNEL f2 ====	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00
PL2	0.00
PL12	16.16
PL13	17.00
PL2W	10.27361584
PL12W	0.24872722
PL13W	0.20498557
SFO2	400.1316005
SI	32768
SF	100.6127690
WDW	EM
SSB	0
LB	3.00
GB	0
PC	1.40

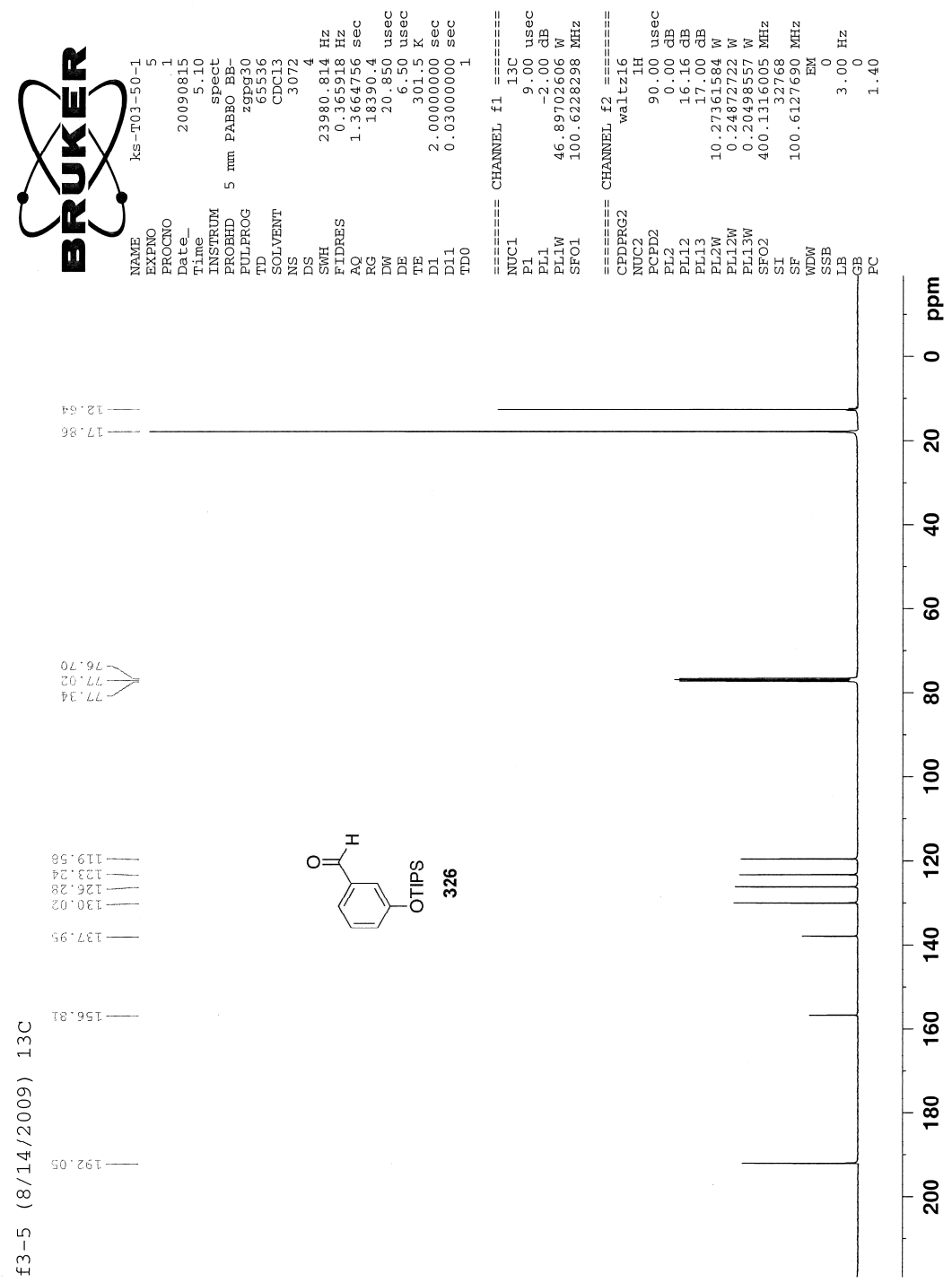

75 (9/15/2009) after column 23.5 mg taken
NAME ks-T03-75-1
EXPNO 3
PROCNO 1
Date_ 20090915
Time 23.12
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 64
DW 78.000 u
DE 6.50 u
TE 301.2 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1328009 M
SI 32768
SF 400.1300000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
7.282
5.009
4.810
4.137
4.120
4.002
3.739
3.553
2.847
2.105
2.073
2.050
1.891
1.750
1.650
1.632
1.494
1.476
1.332
1.313
1.283
1.266
MeO
BocN
Boc
O
112
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm

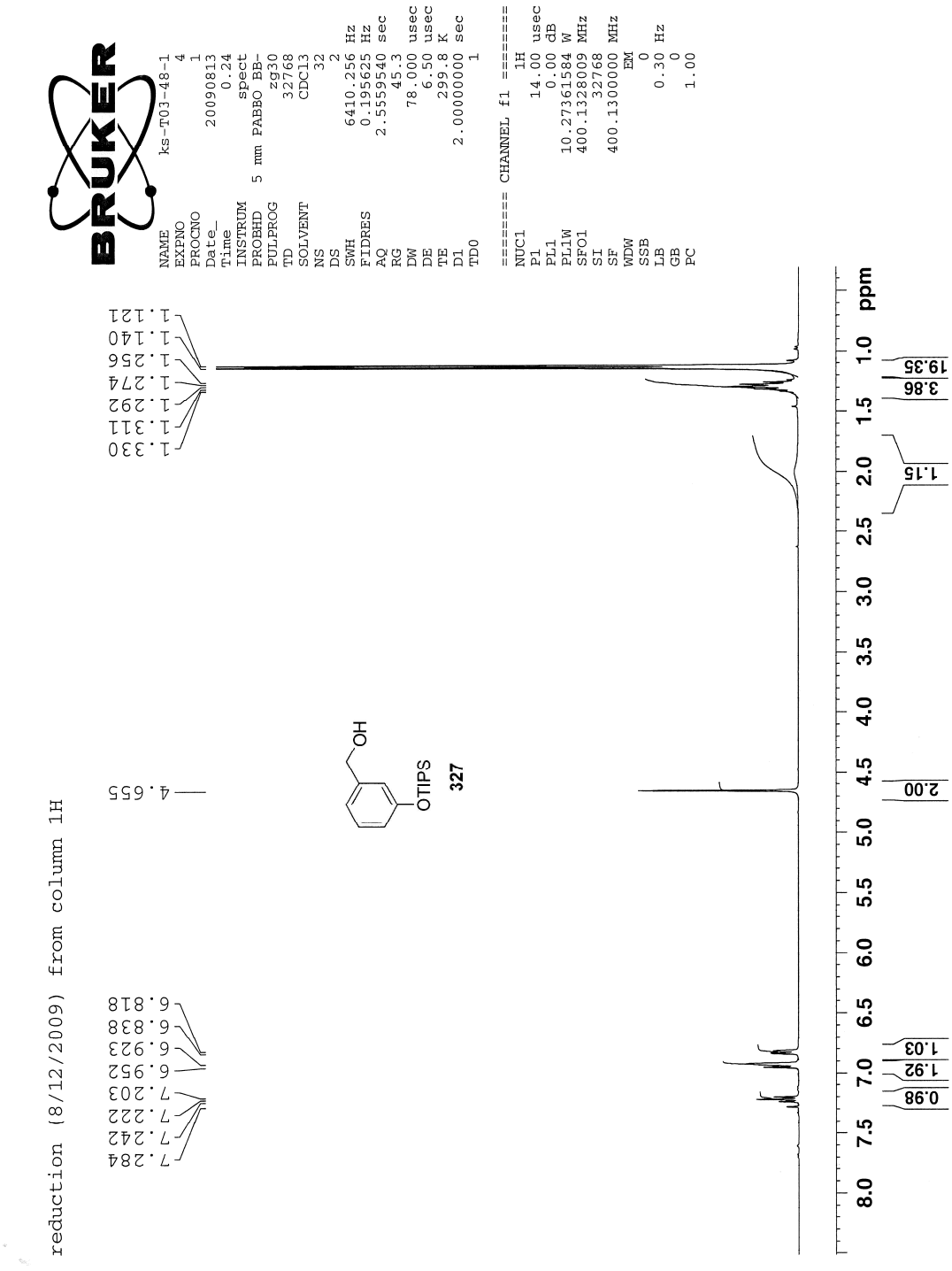

75 (9/15/2009) after column 23.5 mg taken 13C
ks-T03-75-1
NAME 7
EXPNO 1
PROCNO 1
Date_ 20090916
Time 7.07
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4096
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 18390.4
DW 20.850 u
DE 6.50 u
TE 303.5 K
D1 2.00000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
PL1W 46.89702606 W
SFO1 100.6228298 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1316005 M
SI 32768
SF 100.6127690 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
170.42
154.57
154.02
81.67
80.23
77.32
77.00
76.68
60.30
56.26
54.52
51.93
45.01
42.73
31.53
28.20
25.25
24.29
22.59
20.95
20.04
14.15
14.03
MeO
BocN
Boc
O
112
200
180
160
140
120
100
80
60
40
20
0
ppm

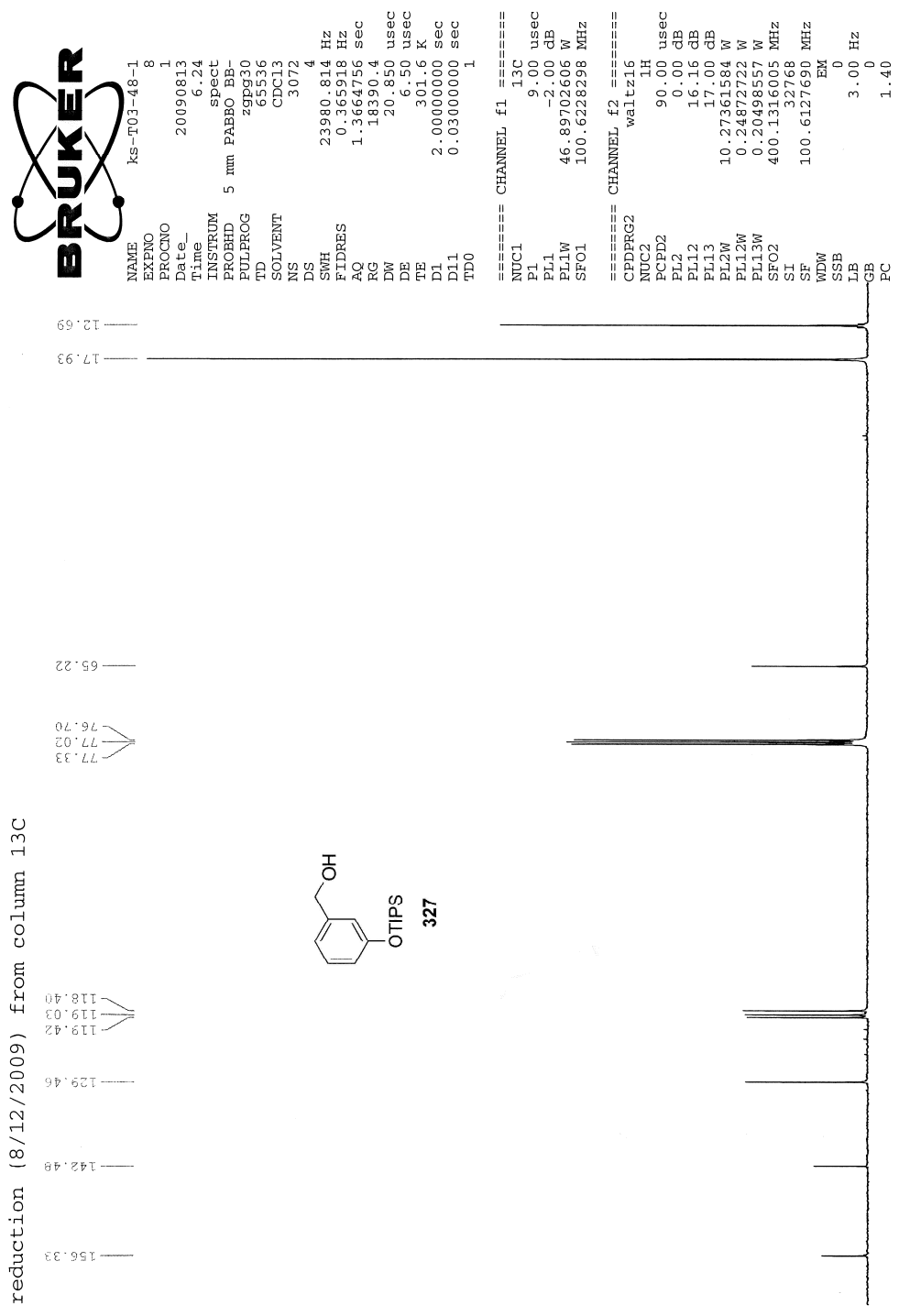

15 crude (10/26/2009) 742.5 mg
7.291
6.201
4.016
3.999
3.990
3.821
3.404
3.389
3.373
3.357
3.345
3.327
3.311
3.296
2.385
2.214
2.202
2.191
2.179
2.006
1.985
1.972
1.963
1.949
1.938
MeO
HN
·2CF3COOH
113
6.46
3.01
1.07
2.05
3.00
1.08
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
NAME ks-T04-15-1
EXPNO 1
PROCNO 1
Date_ 20091026
Time 12.05
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 362
DW 78.000
DE 6.50
TE 301.2
D1 1.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 14.00
PL1 0.00
PL1W 10.27361584
SFO1 400.1378009
SI 32768
SF 400.1350000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

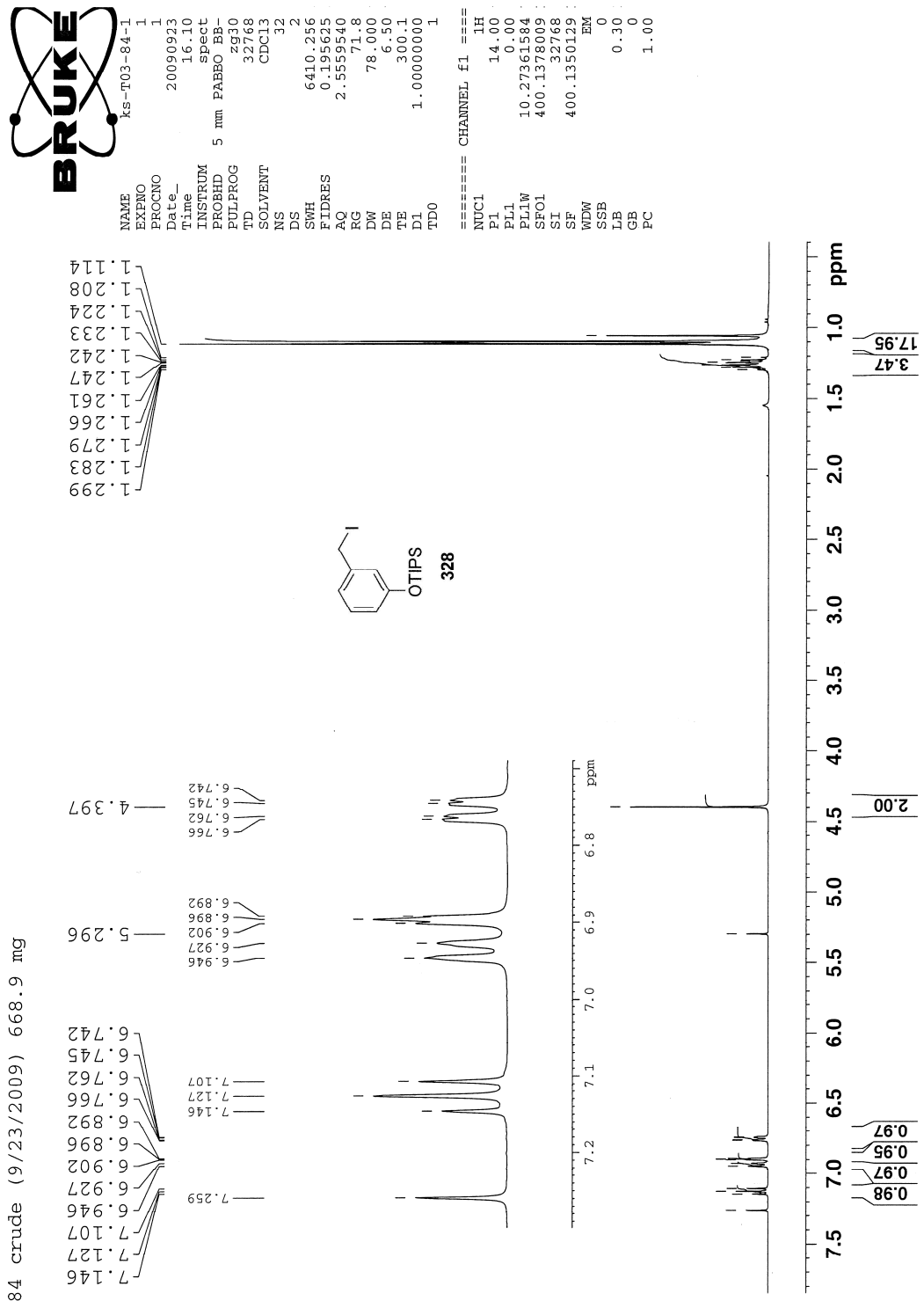

15 crude (10/26/2009) 742.5 mg raken more for NMR 13C
Current Data Parameters
NAME ks-T04-15-1
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20091027
Time 6.49
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3072
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.36647568 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
171.44
77.34
77.03
76.71
55.80
52.77
45.06
29.71
24.70
19.74
MeO
O
HN
H
·2CF3COOH
113
ppm

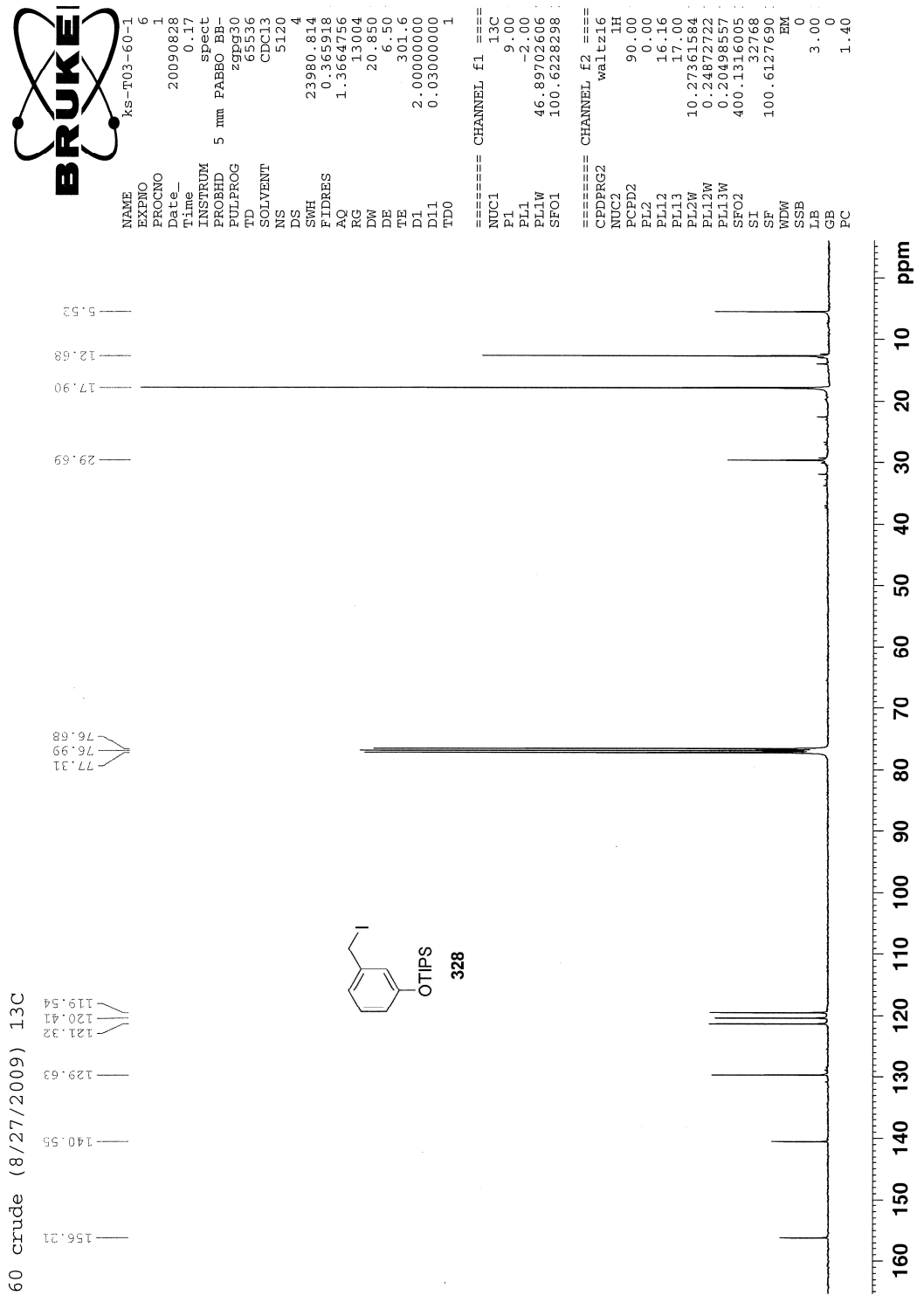

f3-5 (8/14/2009) 1H
OTIPS
326
ppm

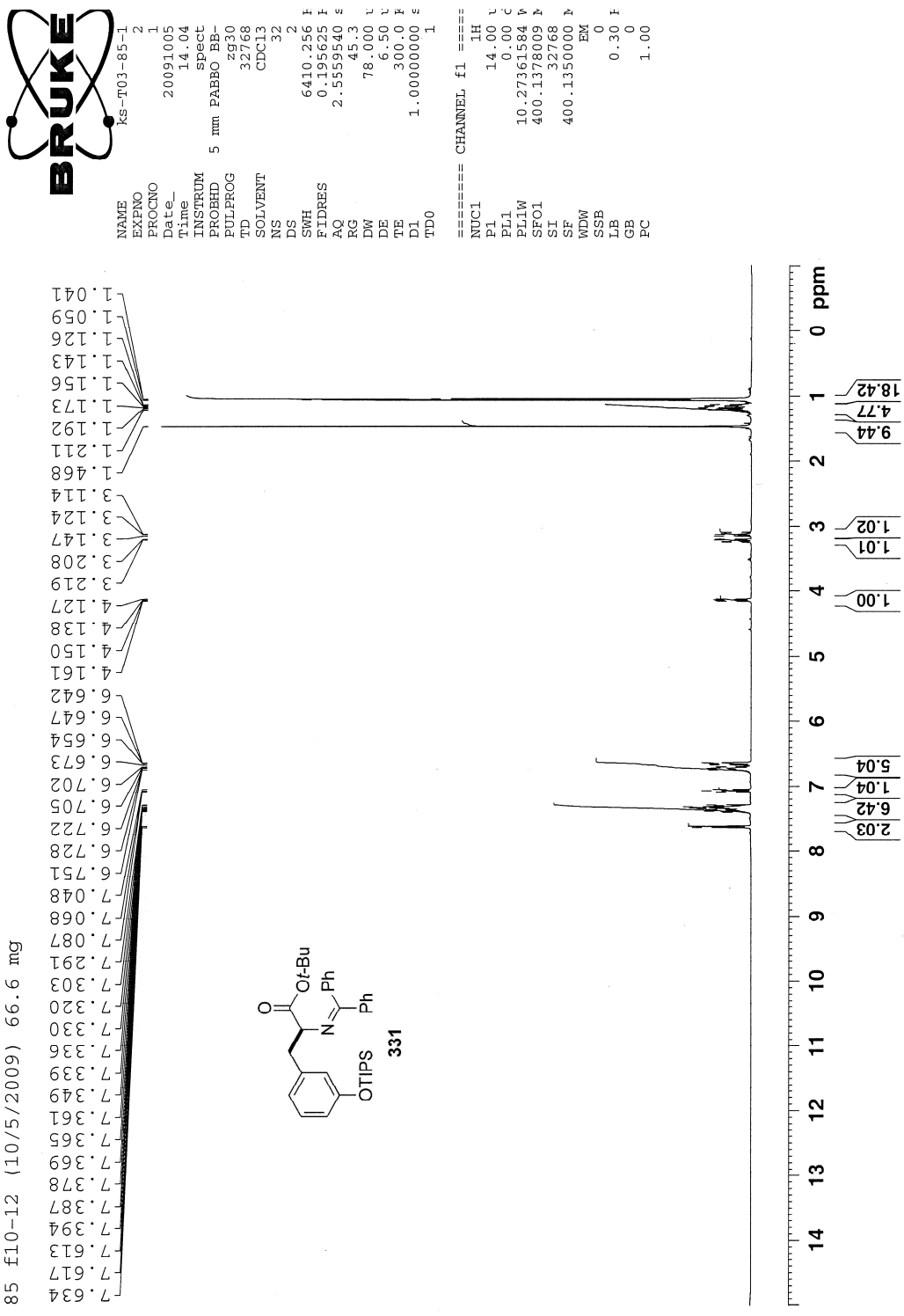

f3-5 (8/14/2009) 13C
OTIPS
326
192.05
156.81
137.95
130.02
126.28
123.24
119.56
77.34
77.02
76.70
17.86
12.64
200
180
160
140
120
100
80
60
40
20
0
ppm

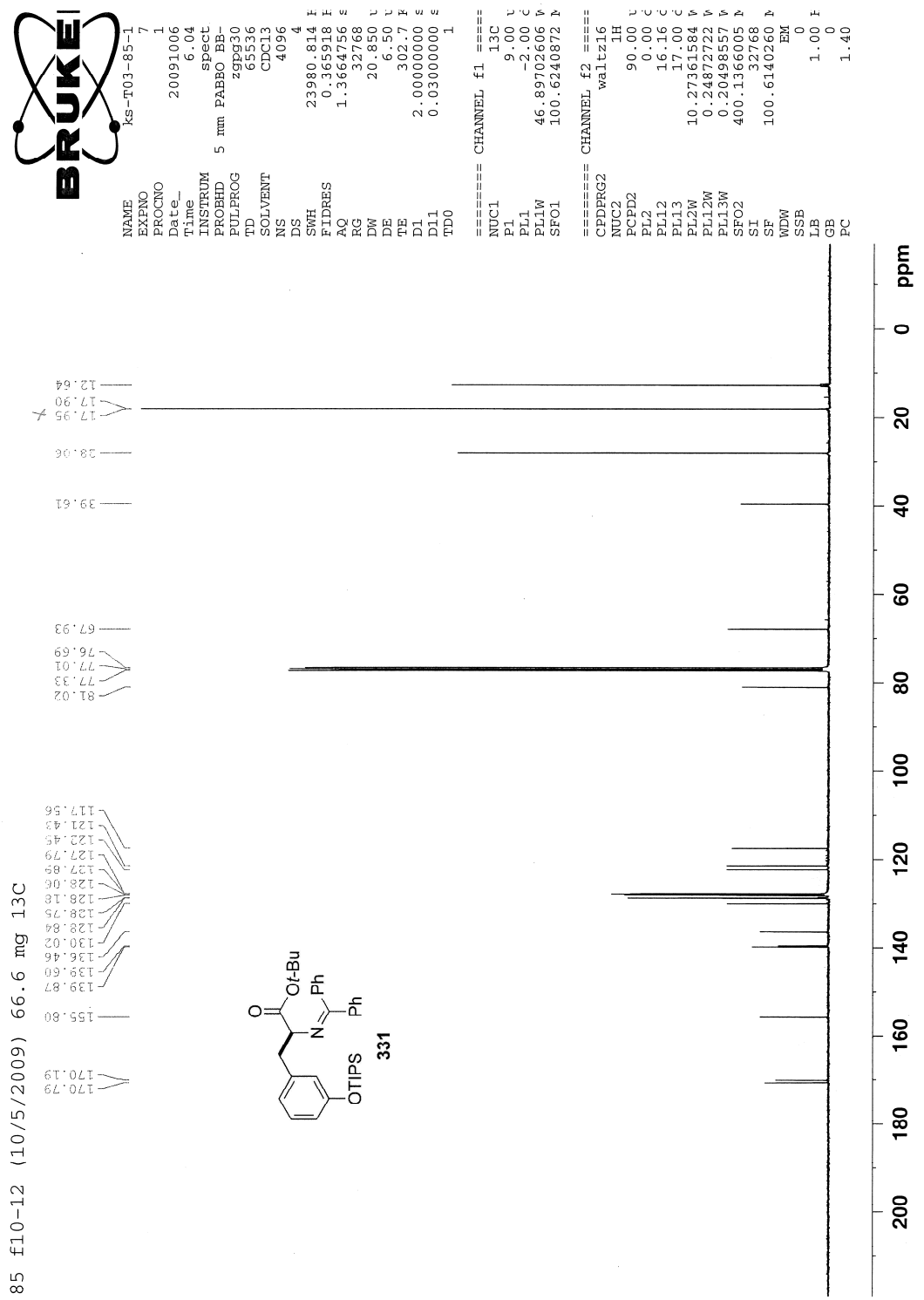

reduction (8/12/2009) from column 1H
NAME ks-TO3-48-1
EXPNO 4
PROCNO 1
Date_ 20090813
Time 0.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.1955625 Hz
AQ 2.5559540 sec
RG 45.3
DW 78.000 usec
DE 6.50 usec
TE 299.8 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1328009 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
OTIPS
327
7.284
7.242
7.222
7.203
6.952
6.923
6.838
6.818
4.655
1.330
1.311
1.292
1.274
1.256
1.140
1.121
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.98
1.92
1.03
2.00
1.15
3.86
19.35

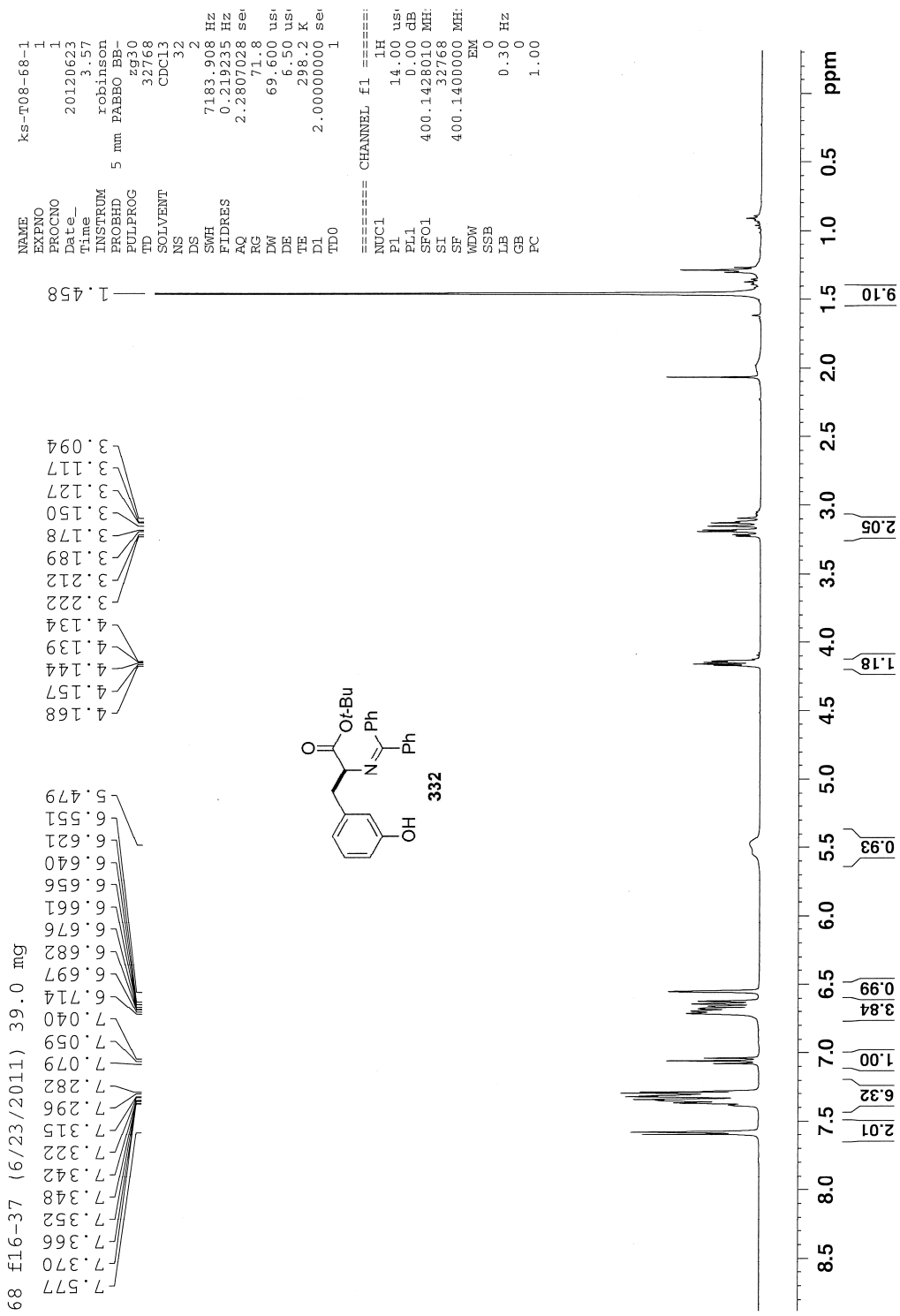

reduction (8/12/2009) from column 13C
OH
OTIPS
327
12.69
17.93
65.22
76.70
77.02
77.33
118.40
119.03
119.42
129.46
142.48
156.33
ppm

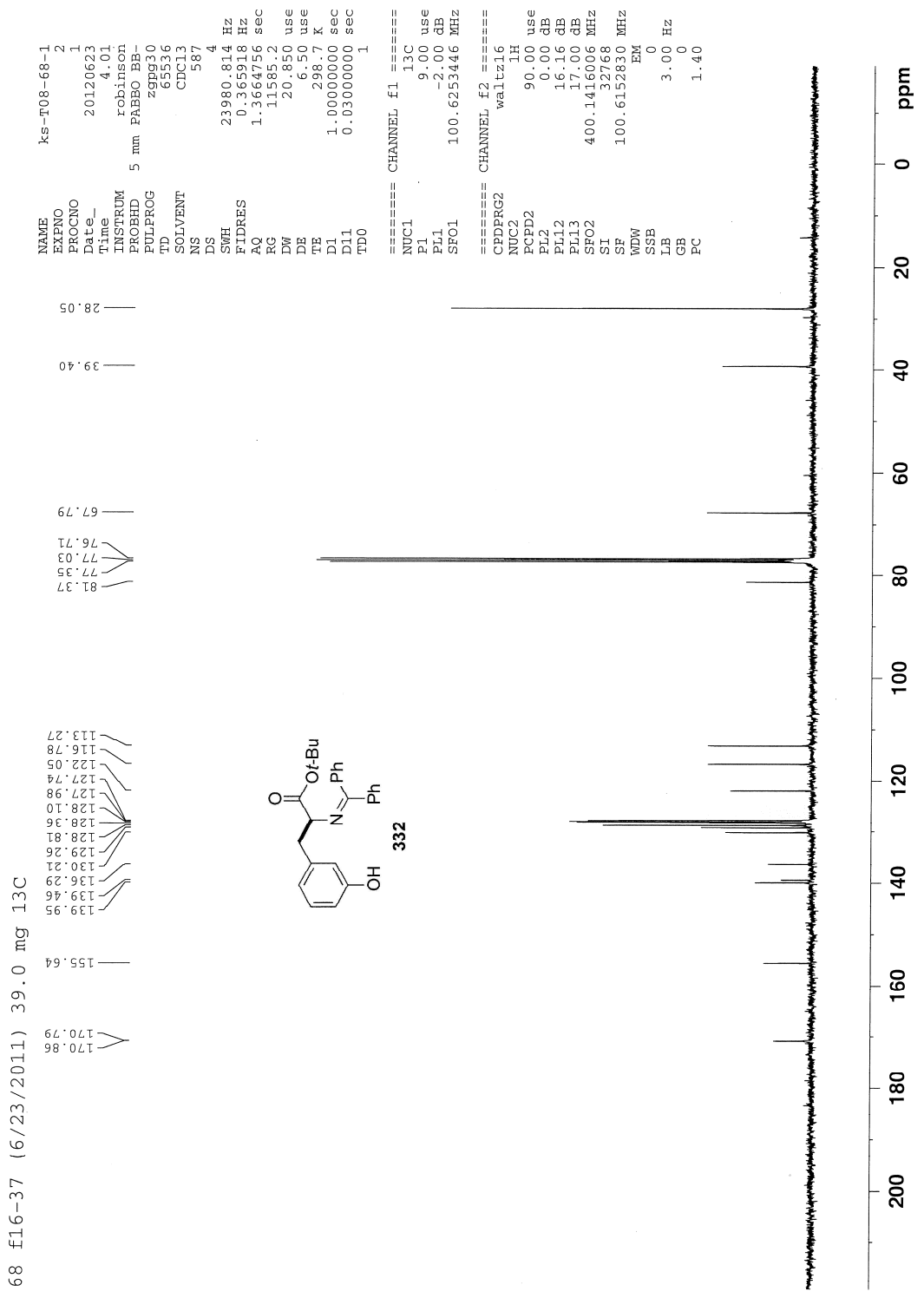

84 crude (9/23/2009) 668.9 mg
NAME ks-T03-84-1
EXPNO 1
PROCNO 1
Date_ 20090923
Time 16.10
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 71.8
DW 78.000
DE 6.50
TE 300.1
D1 1.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 14.00
PL1 0.00
PL1W 10.27361584
SFO1 400.1378009
SI 32768
SF 400.1350129
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
OTIPS
328
ppm
3.47
17.95
2.00
0.98
0.97
0.95
0.97

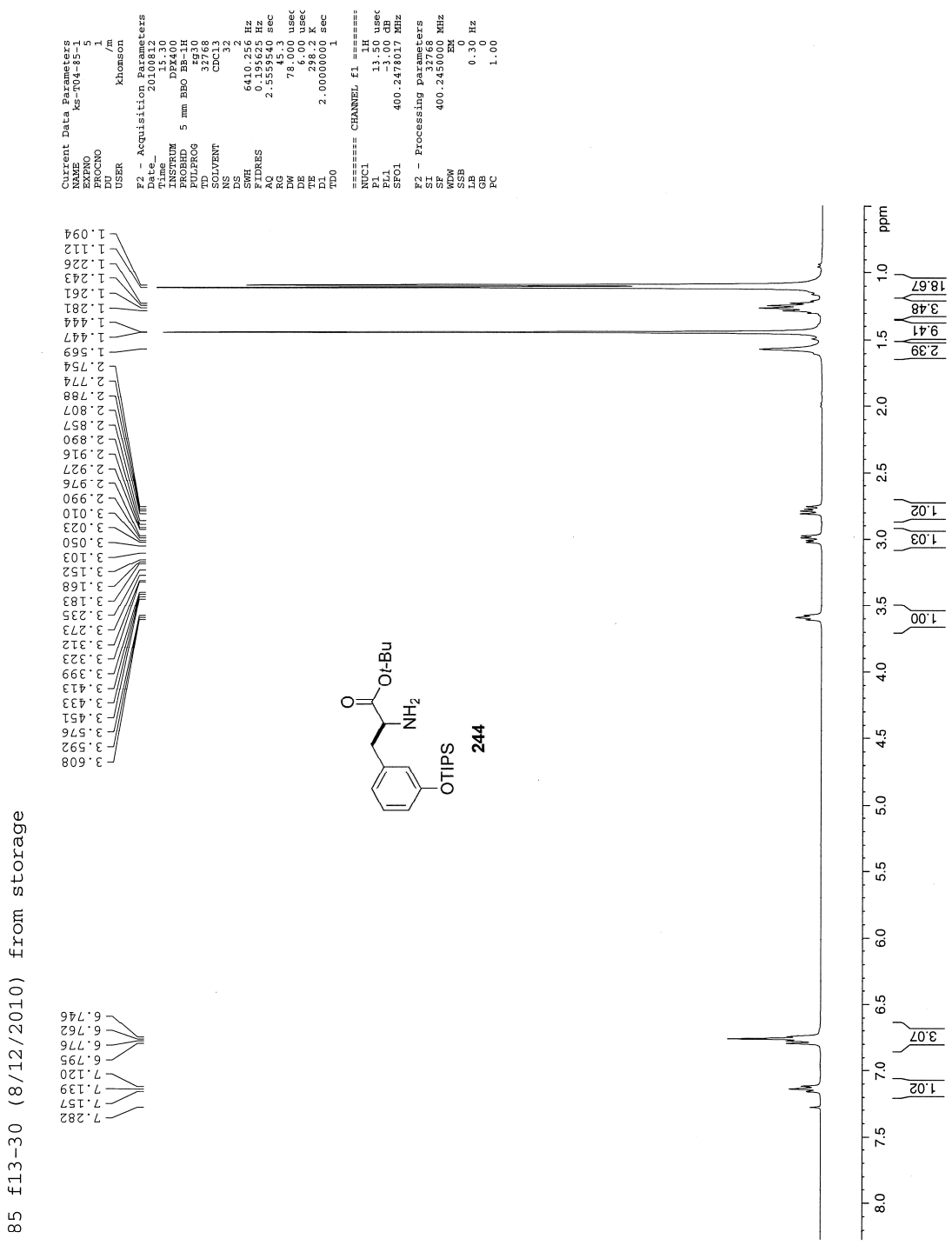

60 crude (8/27/2009) 13C
NAME ks-T03-60-1
EXPNO 6
PROCNO 1
Date_ 20090828
Time_ 0.17
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 5120
DS 4
SWH 23980.814
FIDRES 0.365918
AQ 1.3664756
RG 13004
DW 20.850
DE 6.50
TE 301.6
D1 2.00000000
D11 0.03000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 9.00
PL1 -2.00
PL1W 46.89702606
SFO1 100.6228298
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00
PL2 0.00
PL12 16.16
PL13 17.00
PL2W 10.27361584
PL12W 0.24872722
PL13W 0.20498557
SFO2 400.1316005
SI 32768
SF 100.6127690
WDW EM
SSB 0
LB 3.00
GB 0
PC 1.40
156.21
140.55
129.63
121.32
120.41
119.54
77.31
76.99
76.68
29.69
17.90
12.68
5.52
OTIPS
328
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

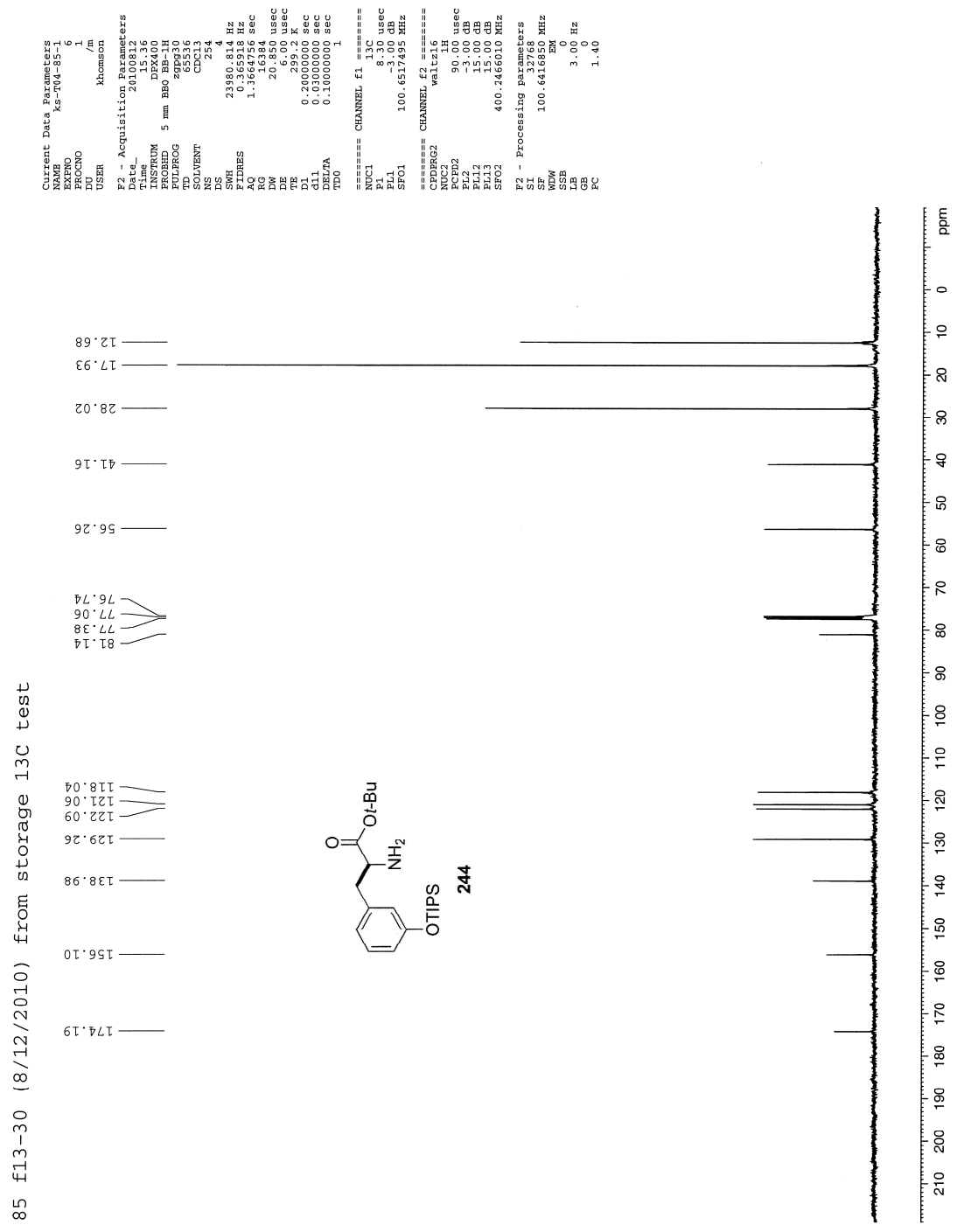

85 f10-12 (10/5/2009) 66.6 mg
ks-T03-85-1
NAME
EXPNO
PROCNO
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
TD0
CHANNEL f1
NUC1
P1
PL1
PL1W
SFO1
SI
SF
WDW
SSB
LB
GB
PC
O
Ot-Bu
Ph
N
Ph
OTIPS
331
ppm
18.42
4.77
9.44
1.02
1.01
1.00
5.04
1.04
6.42
2.03

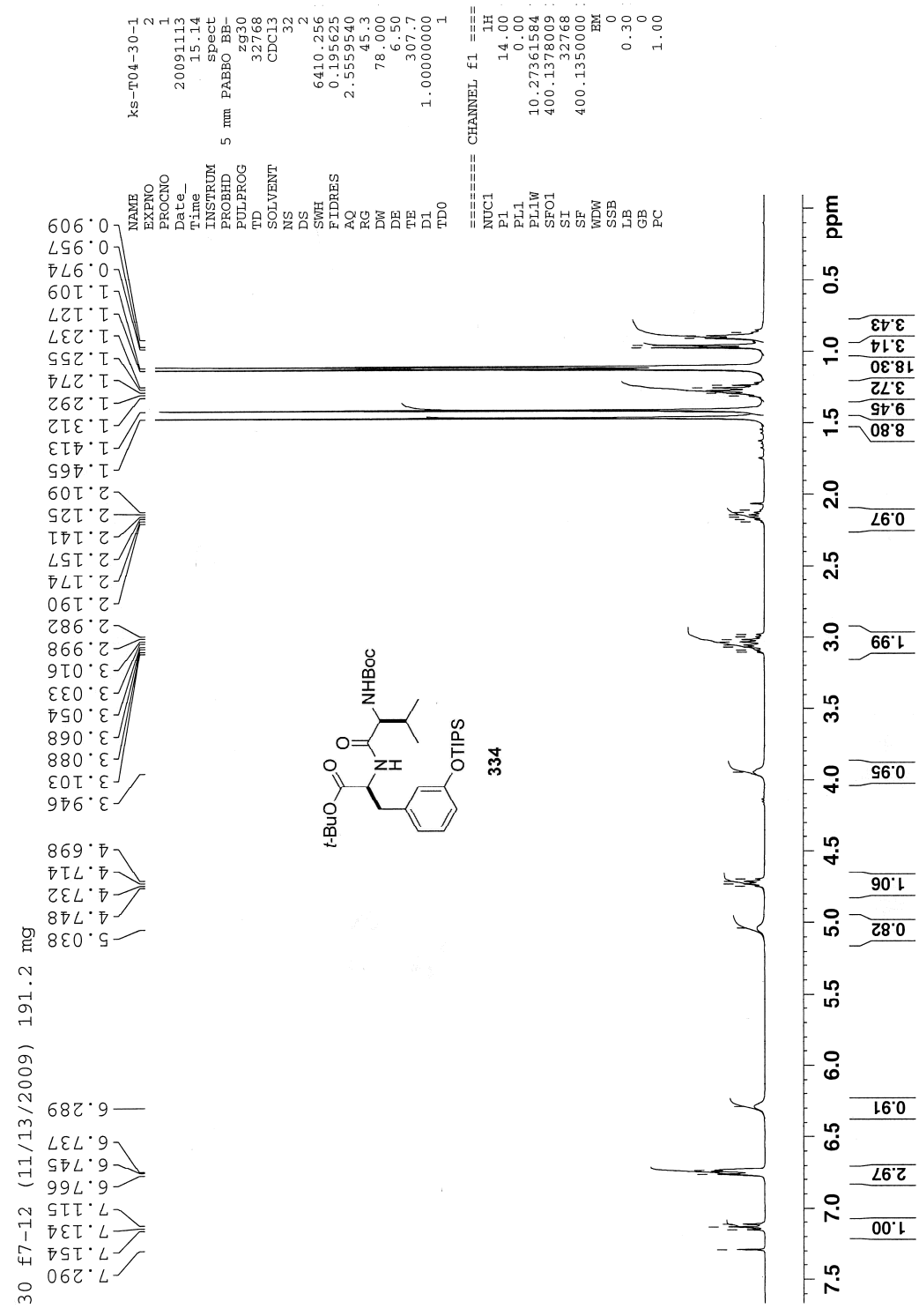

85 f10-12 (10/5/2009) 66.6 mg 13C
ks-T03-85-1
NAME
EXPNO 7
PROCNO 1
Date_ 20091006
Time_ 6.04
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4096
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 32768
DW 20.850 u
DE 6.50 u
TE 302.7 K
D1 2.00000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
PL1W 46.89702606 W
SFO1 100.6240872 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1366005 M
SI 32768
SF 100.6140260 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
12.64
17.80
17.95
38.06
39.61
67.93
76.69
77.01
77.33
81.02
117.56
121.43
122.45
127.79
127.89
128.06
128.18
128.75
128.84
130.02
136.46
139.60
139.87
155.60
170.19
170.79
O
Ot-Bu
N
Ph
Ph
OTIPS
331
200
180
160
140
120
100
80
60
40
20
0
ppm

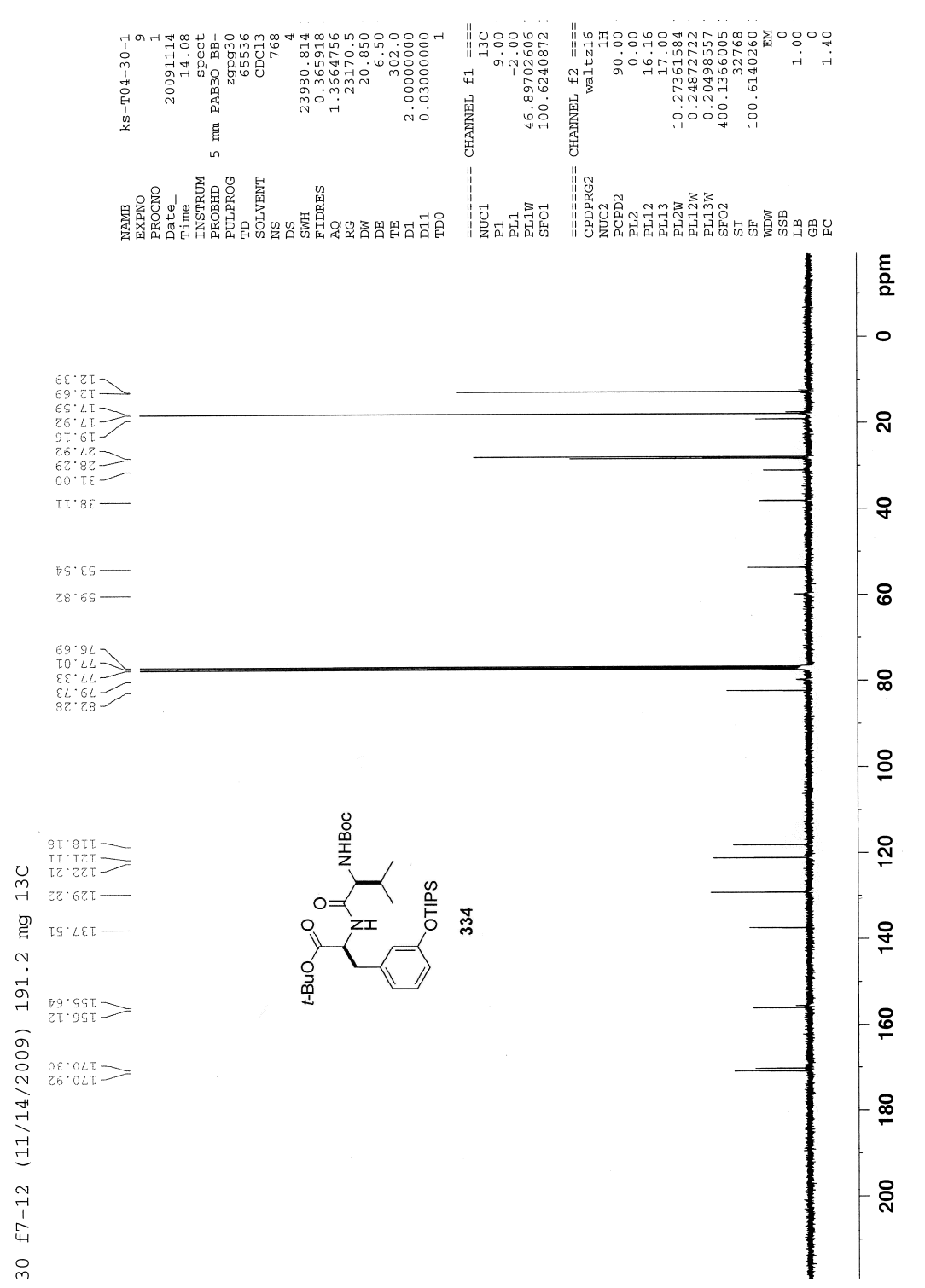

68 f16-37 (6/23/2011) 39.0 mg
NAME ks-T08-68-1
EXPNO 1
PROCNO 1
Date_ 20120623
Time 3.57
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 7183.908 Hz
FIDRES 0.219235 Hz
AQ 2.2807028 se
RG 71.8
DW 69.600 us
DE 6.50 us
TE 298.2 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
SFO1 400.1428010 MH
SI 32768
SF 400.1400000 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
Ot-Bu
Ph
N
Ph
OH
332
ppm
9.10
2.05
1.18
0.93
3.84
0.99
1.00
6.32
2.01

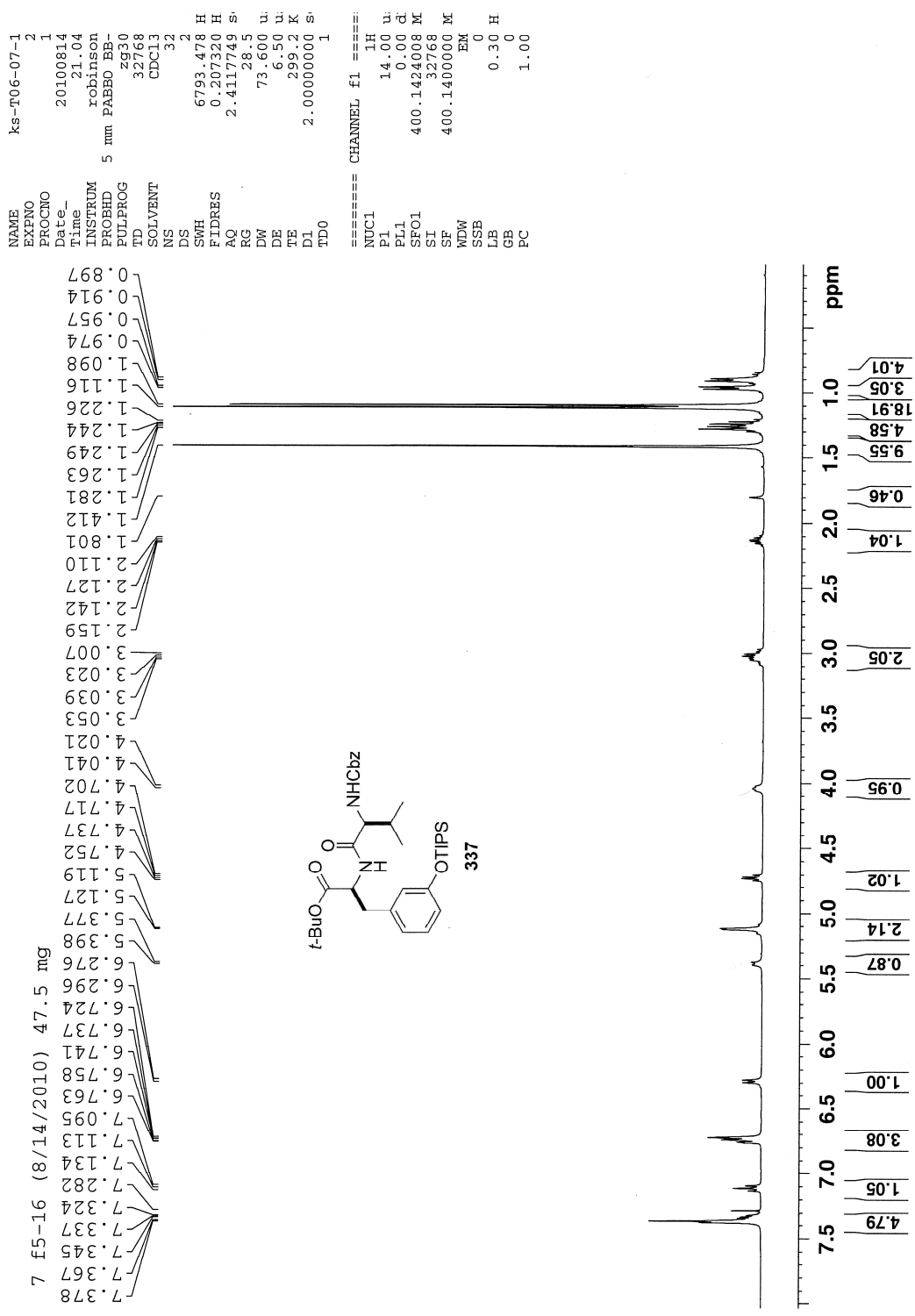

68 f16-37 (6/23/2011) 39.0 mg 13C
NAME ks-T08-68-1
EXPNO 2
PROCNO 1
Date_ 20120623
Time 4.01
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 587
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 11585.2
DW 20.850 use
DE 6.50 use
TE 298.7 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 use
PL1 -2.00 dB
SFO1 100.6253446 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 0.00 dB
PL12 16.16 dB
PL13 17.00 dB
SFO2 400.1416006 MHz
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
170.86
170.79
155.64
139.95
139.46
136.29
130.21
129.26
128.81
128.36
128.10
127.98
127.74
122.05
116.78
113.27
81.37
77.35
77.03
76.71
67.79
39.40
28.05
O
Ot-Bu
N
Ph
Ph
OH
332
200
180
160
140
120
100
80
60
40
20
0
ppm

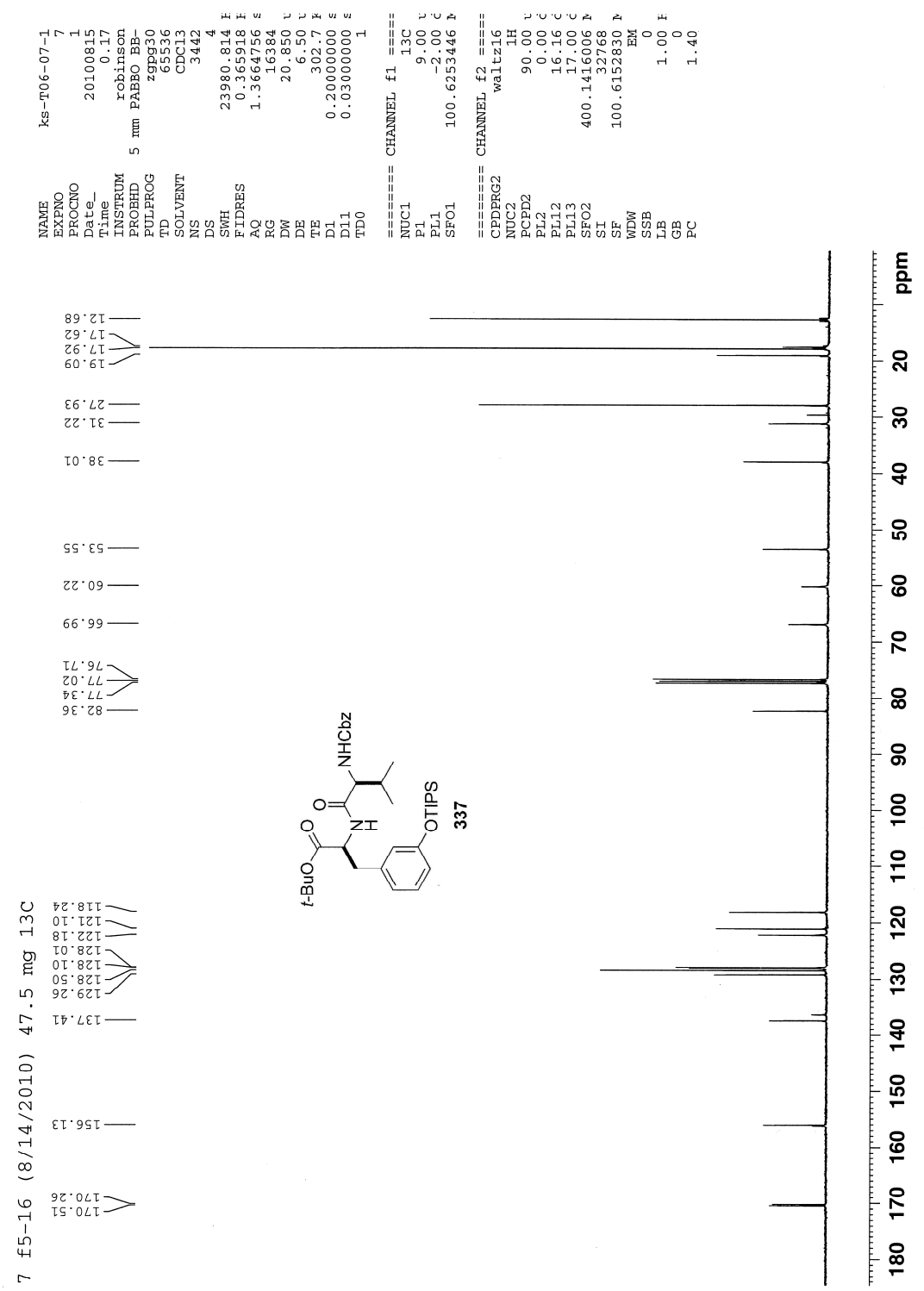

85 f13-30 (8/12/2010) from storage
Current Data Parameters
NAME ks-T04-85-1
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100812
Time 15.30
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 37768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55559540 sec
RG 45.3
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -1.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.3 Hz
GB 0
PC 1.00
O
O-t-Bu
NH2
OTIPS
244
ppm
2.39
9.41
3.48
18.67
1.03
1.02
1.00
3.07
1.02

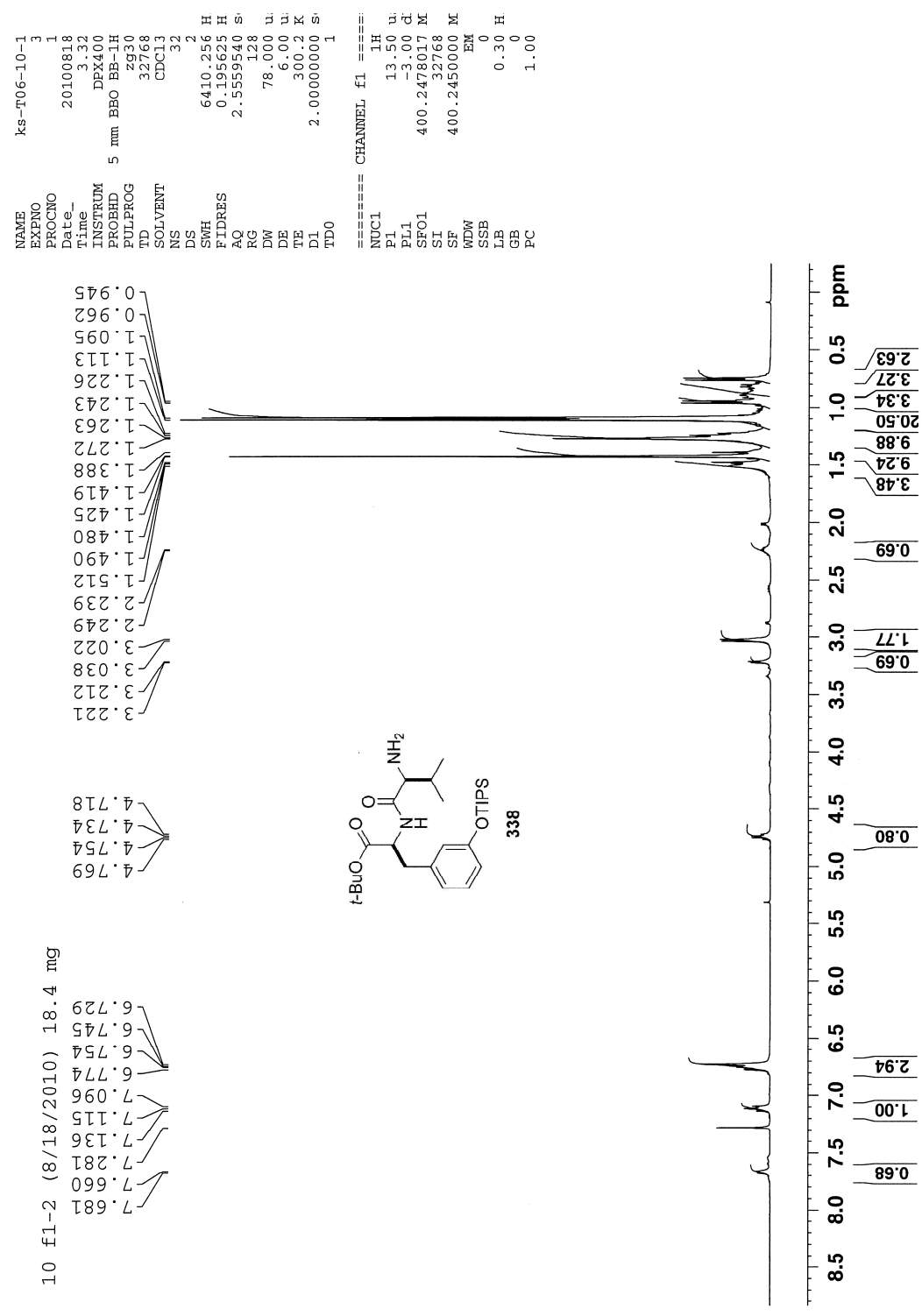

85 f13-30 (8/12/2010) from storage 13C test
Current Data Parameters
NAME ks-T04-85-1
EXPNO 6
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20100812
Time 15.38
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 254
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.36644756 sec
RG 16384
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
12.68
17.93
28.02
41.16
56.26
76.74
77.06
77.38
81.14
118.04
121.06
122.09
129.26
138.98
156.10
174.19
O
Ot-Bu
NH2
OTIPS
244
ppm

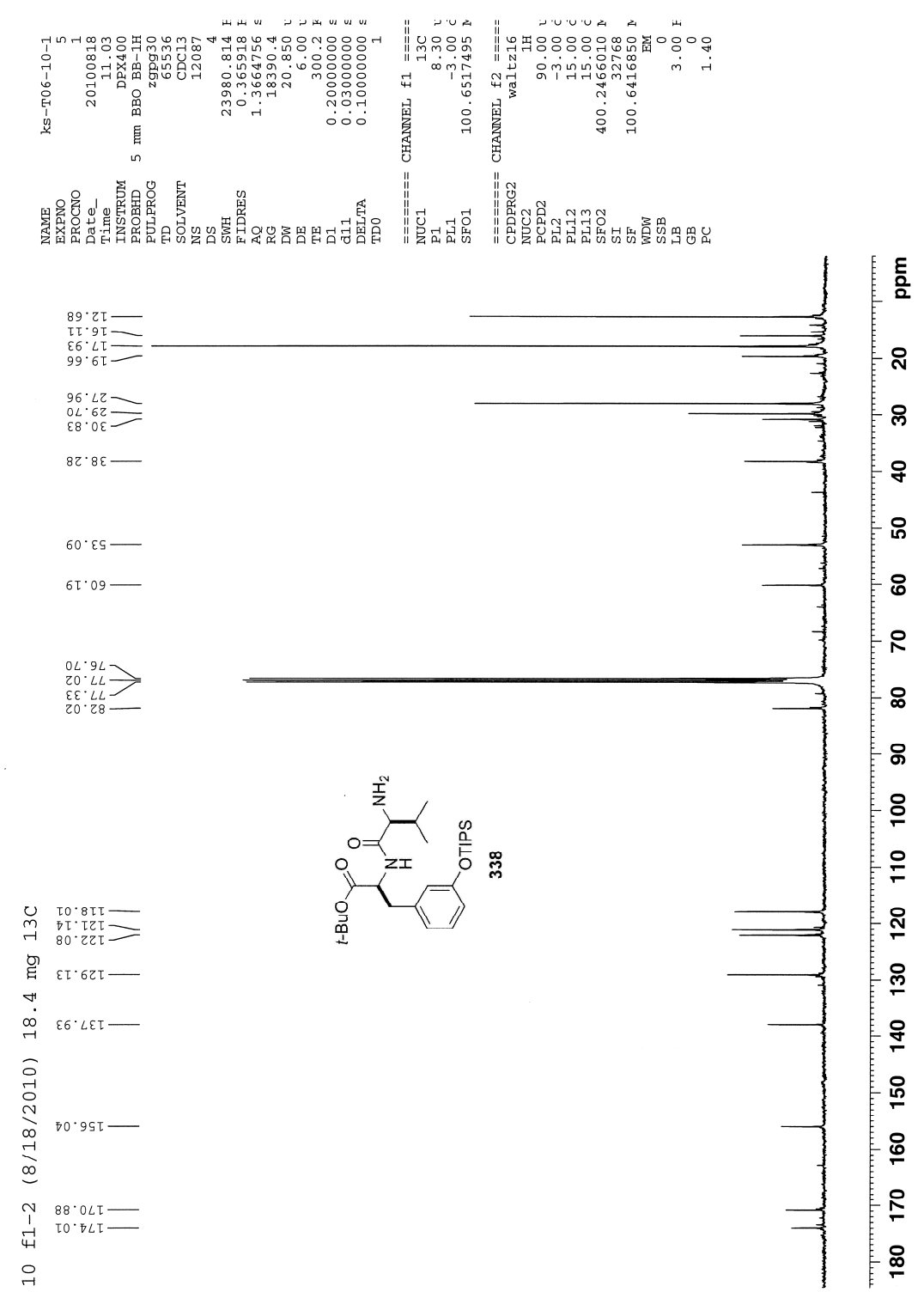

30 f7-12 (11/13/2009) 191.2 mg
NAME ks-T04-30-1
EXPNO 2
PROCNO 1
Date_ 20091113
Time 15.14
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 45.3
DW 78.000
DE 6.50
TE 307.7
D1 1.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 14.00
PL1 0.00
PL1W 10.27361584
SFO1 400.1378009
SI 32768
SF 400.1350000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
NHBoc
O
O
N
H
t-BuO
OTIPS
334
ppm
0.909
0.957
0.974
1.109
1.127
1.237
1.255
1.274
1.292
1.312
1.413
1.465
2.109
2.125
2.141
2.157
2.174
2.190
2.982
2.998
3.016
3.033
3.054
3.068
3.088
3.103
3.946
4.698
4.714
4.732
4.748
5.038
6.289
6.737
6.745
6.766
7.115
7.134
7.154
7.290
8.80
9.45
3.72
18.30
3.14
3.43
0.97
1.99
0.95
1.06
0.82
0.91
2.97
1.00

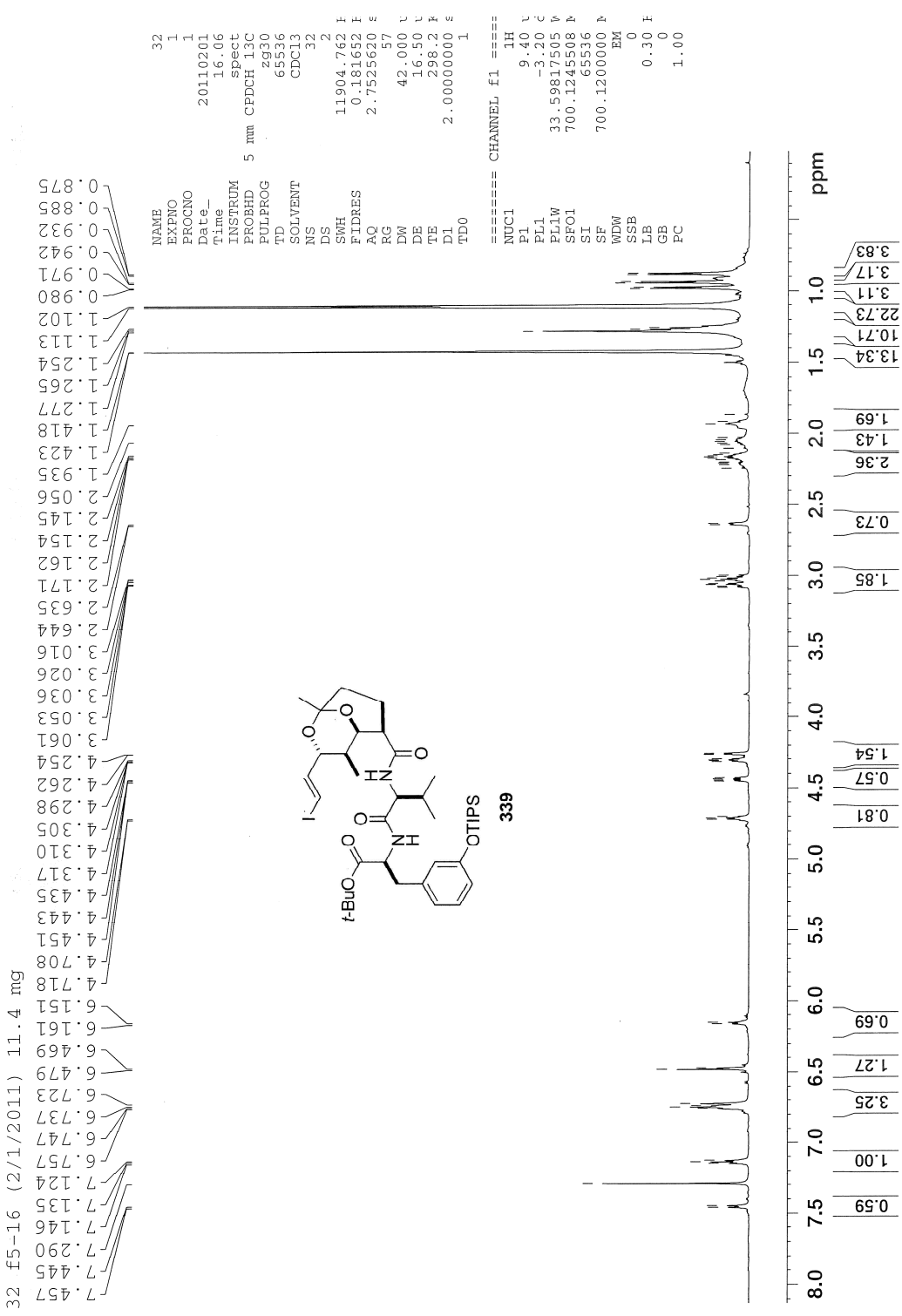

30 f7-12 (11/14/2009) 191.2 mg 13C
170.92
170.30
156.12
155.64
137.51
129.22
122.21
121.11
118.18
82.28
79.73
77.33
77.01
76.69
59.82
53.54
38.11
31.00
28.29
27.92
19.16
17.92
17.59
12.69
12.39
NAME ks-T04-30-1
EXPNO 9
PROCNO 1
Date_ 20091114
Time_ 14.08
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 768
DS 4
SWH 23980.814
FIDRES 0.365918
AQ 1.3664756
RG 23170.5
DW 20.850
DE 6.50
TE 302.0
D1 2.00000000
D11 0.03000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 9.00
PL1 -2.00
PL1W 46.89702606
SFO1 100.6240872
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00
PL2 0.00
PL12 16.16
PL13 17.00
PL2W 10.27361584
PL12W 0.24872722
PL13W 0.20498557
SFO2 400.1366005
SI 32768
SF 100.6140260
WDW EM
SSB 0
LB 1.00
GB 0
PC 1.40
t-BuO
O
O
N
H
NHBoc
OTIPS
334
200
180
160
140
120
100
80
60
40
20
0
ppm

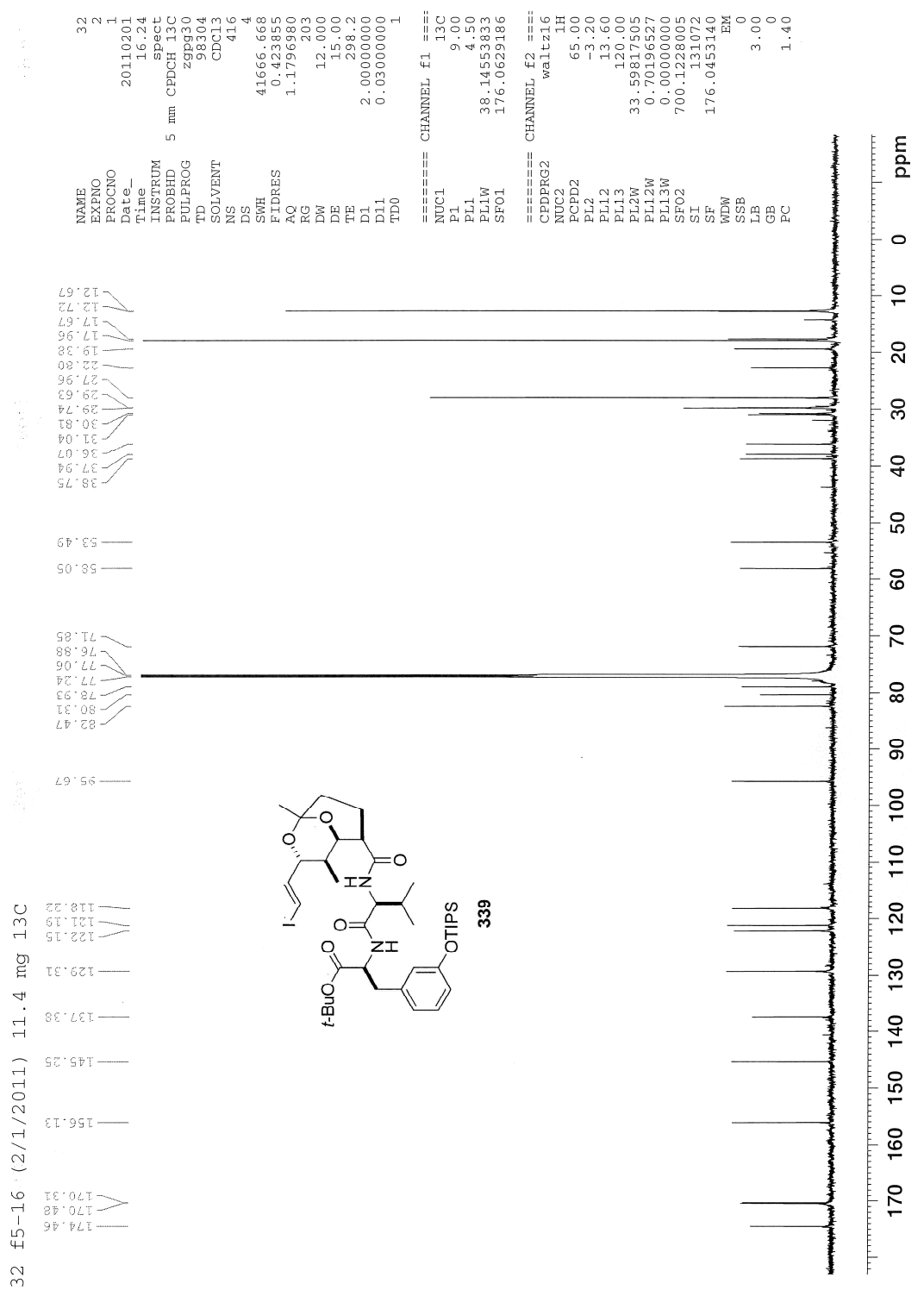

NAME ks-T06-07-1
EXPNO 2
PROCNO 1
Date_ 20100814
Time 21.04
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 28.5
DW 73.600 u
DE 6.50 u
TE 299.2 K
D1 2.00000000 s
TDO 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
7 f5-16 (8/14/2010) 47.5 mg
t-BuO
NHCbz
OTIPS
337
ppm
4.79
1.05
3.08
1.00
6.5
7.0
7.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.87
2.14
1.02
0.95
2.05
1.04
0.46
9.55
4.58
18.91
3.05
4.01

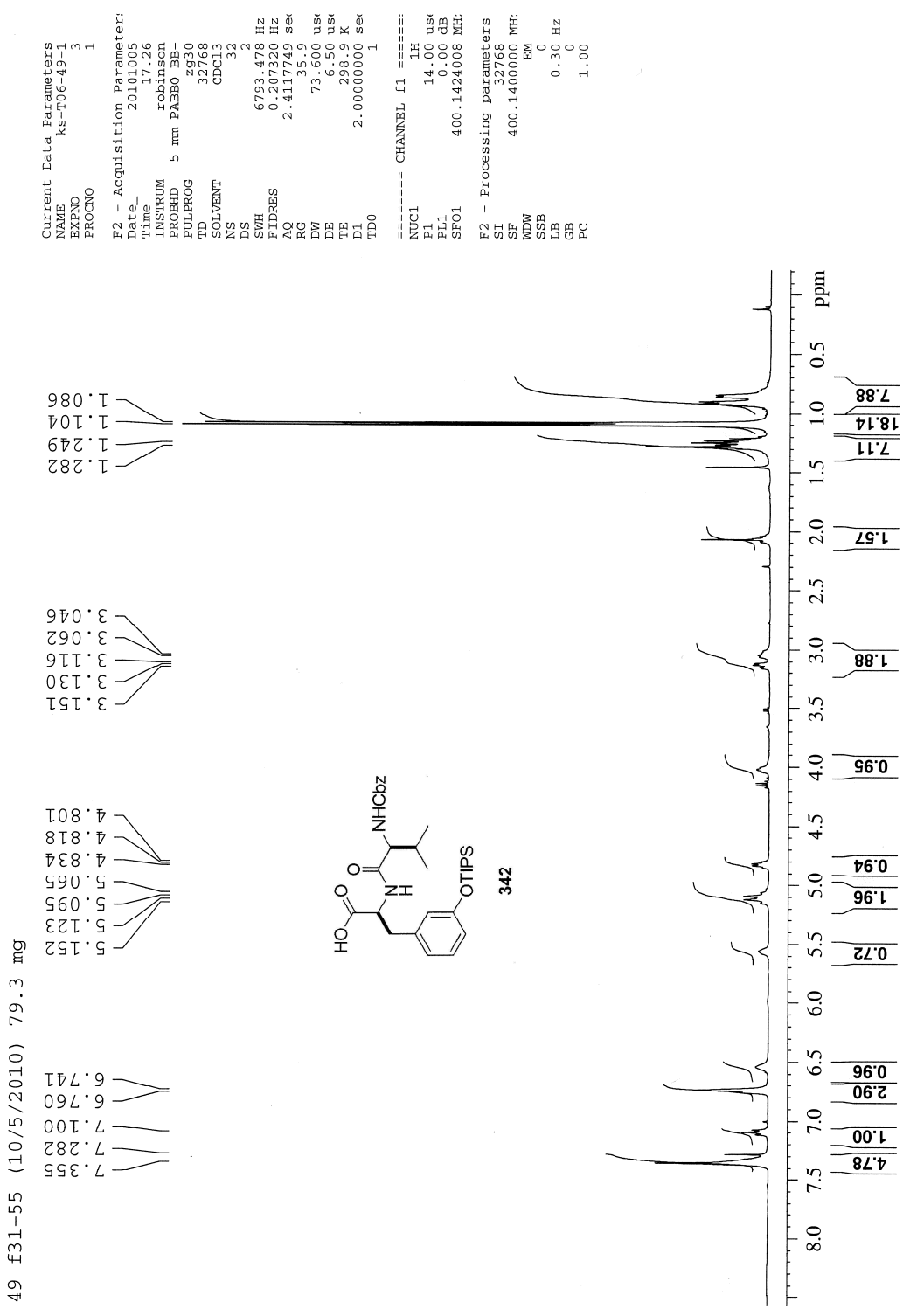

7 f5-16 (8/14/2010) 47.5 mg 13C
NAME ks-T06-07-1
EXPNO 7
PROCNO 1
Date_ 20100815
Time 0.17
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3442
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 16384
DW 20.850 u
DE 6.50 u
TE 302.7 K
D1 0.20000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
SFO1 100.6253446 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
SFO2 400.1416006 M
SI 32768
SF 100.6152830 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
12.68
17.62
17.92
19.09
27.93
31.22
38.01
53.55
60.22
66.99
76.71
77.02
77.34
82.36
118.24
121.10
122.18
128.01
128.10
128.50
129.26
137.41
156.13
170.26
170.51
t-BuO
O
O
NH
NHCbz
OTIPS
337
ppm

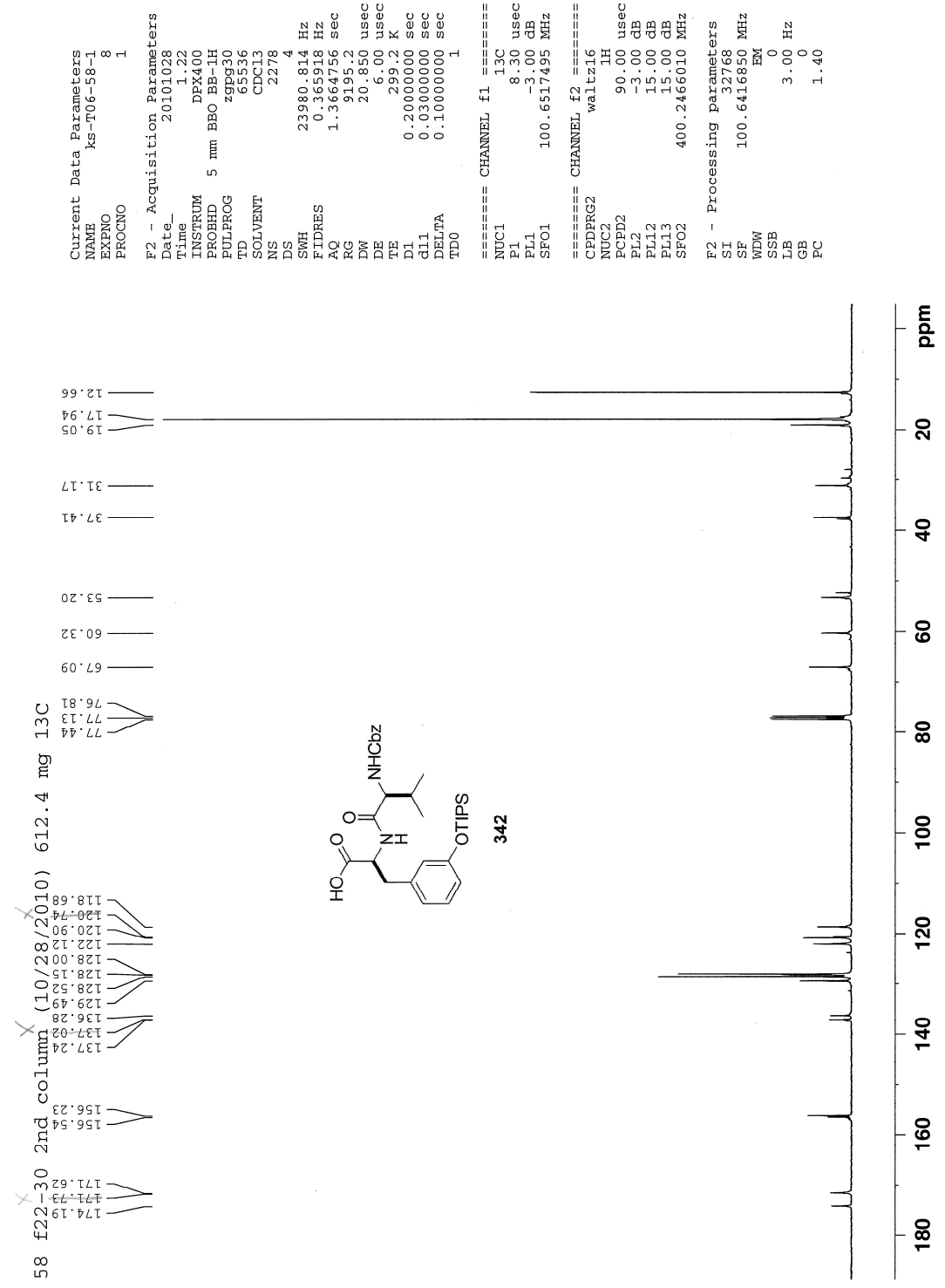

NAME ks-T06-10-1
EXPNO 3
PROCNO 1
Date_ 20100818
Time_ 3.32
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 128
DW 78.000 u
DE 6.00 u
TE 300.2 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 u
PL1 -3.00 d
SFO1 400.2478017 M
SI 32768
SF 400.2450000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
10 f1-2 (8/18/2010) 18.4 mg
7.681
7.660
7.281
7.136
7.115
7.096
6.774
6.754
6.745
6.729
4.769
4.754
4.734
4.718
3.221
3.212
3.038
3.022
2.249
2.239
1.512
1.490
1.480
1.425
1.419
1.388
1.272
1.263
1.243
1.226
1.113
1.095
0.962
0.945
t-BuO
O
NH2
H
N
O
OTIPS
338
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.68
1.00
2.94
0.80
0.69
1.77
0.69
3.48
9.24
9.88
20.50
3.34
3.27
2.63

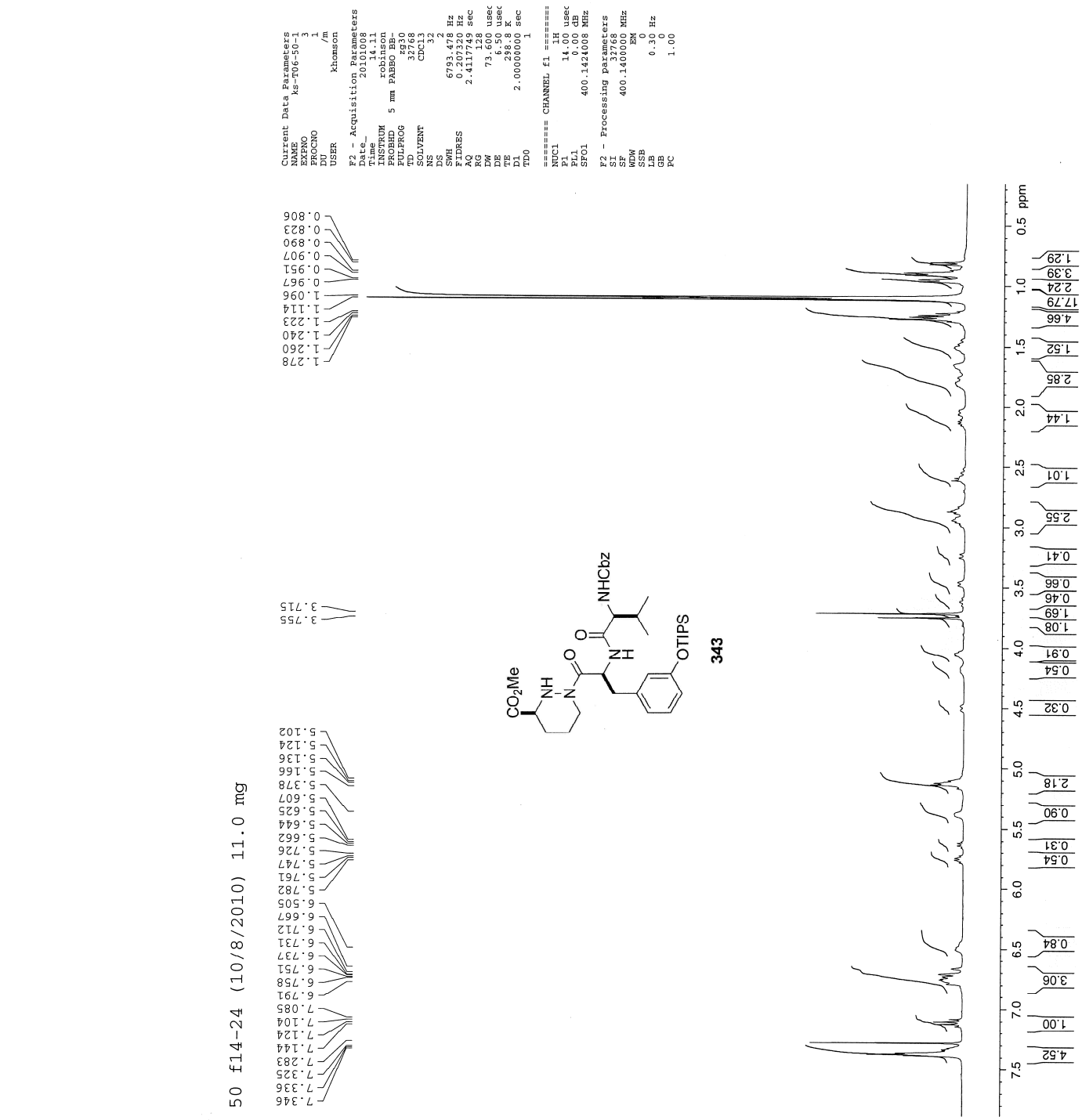

10 f1-2 (8/18/2010) 18.4 mg 13C
NAME ks-T06-10-1
EXPNO 5
PROCNO 1
Date_ 20100818
Time 11.03
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 12087
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 18390.4
DW 20.850 u
DE 6.00 u
TE 300.2 K
D1 0.20000000 s
d11 0.03000000 s
DELTA 0.10000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 8.30 u
PL1 -3.00 d
SFO1 100.6517495 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 -3.00 d
PL12 15.00 d
PL13 15.00 d
SFO2 400.2466010 M
SI 32768
SF 100.6416850 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
12.68
16.11
17.93
19.66
27.96
29.70
30.83
38.28
53.09
60.19
76.70
77.02
77.33
82.02
118.01
121.14
122.08
129.13
137.93
156.04
170.88
174.01
t-BuO
O
O
N
H
NH2
OTIPS
338
ppm

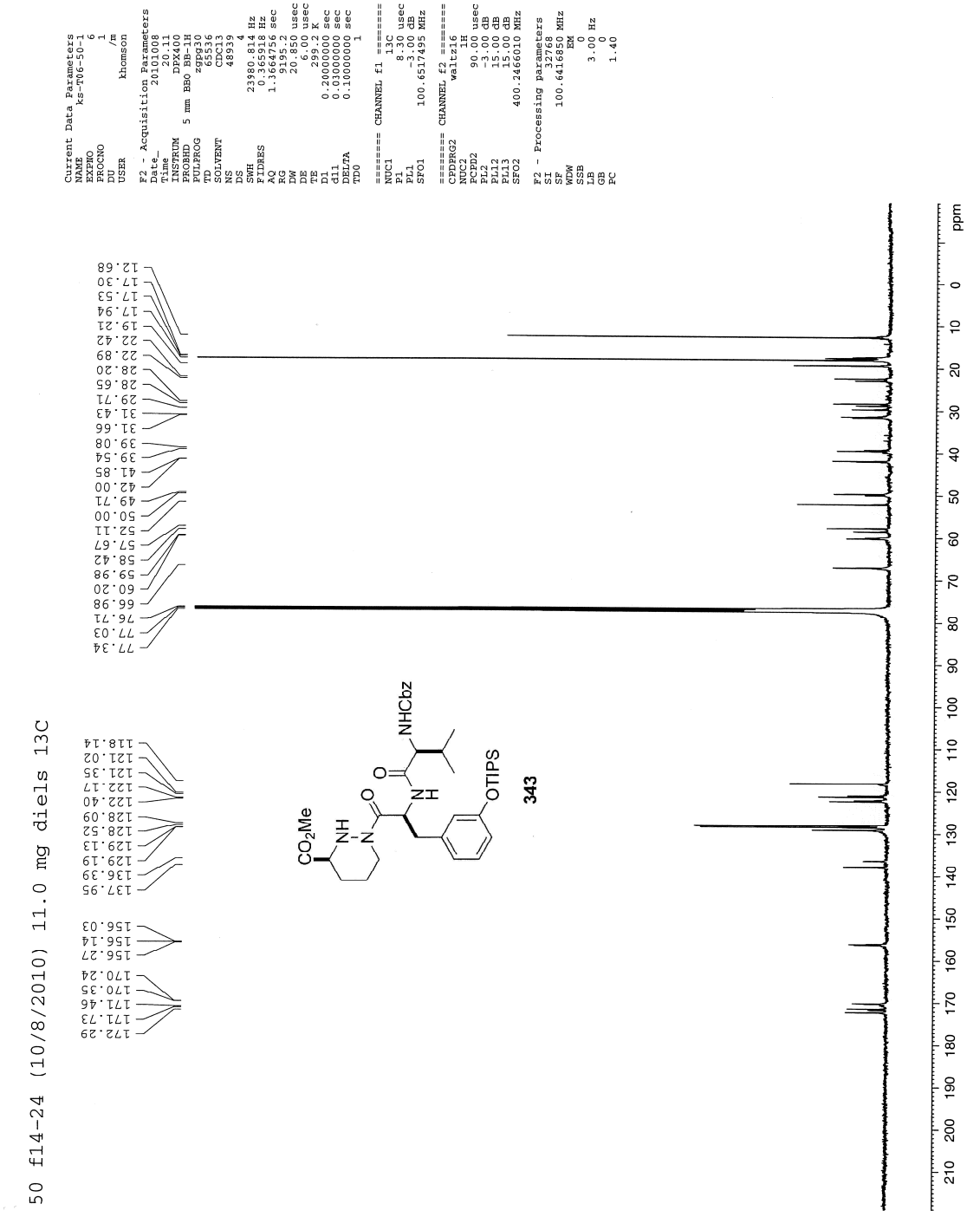

32 f5-16 (2/1/2011) 11.4 mg
339
OTIPS
t-BuO
ppm

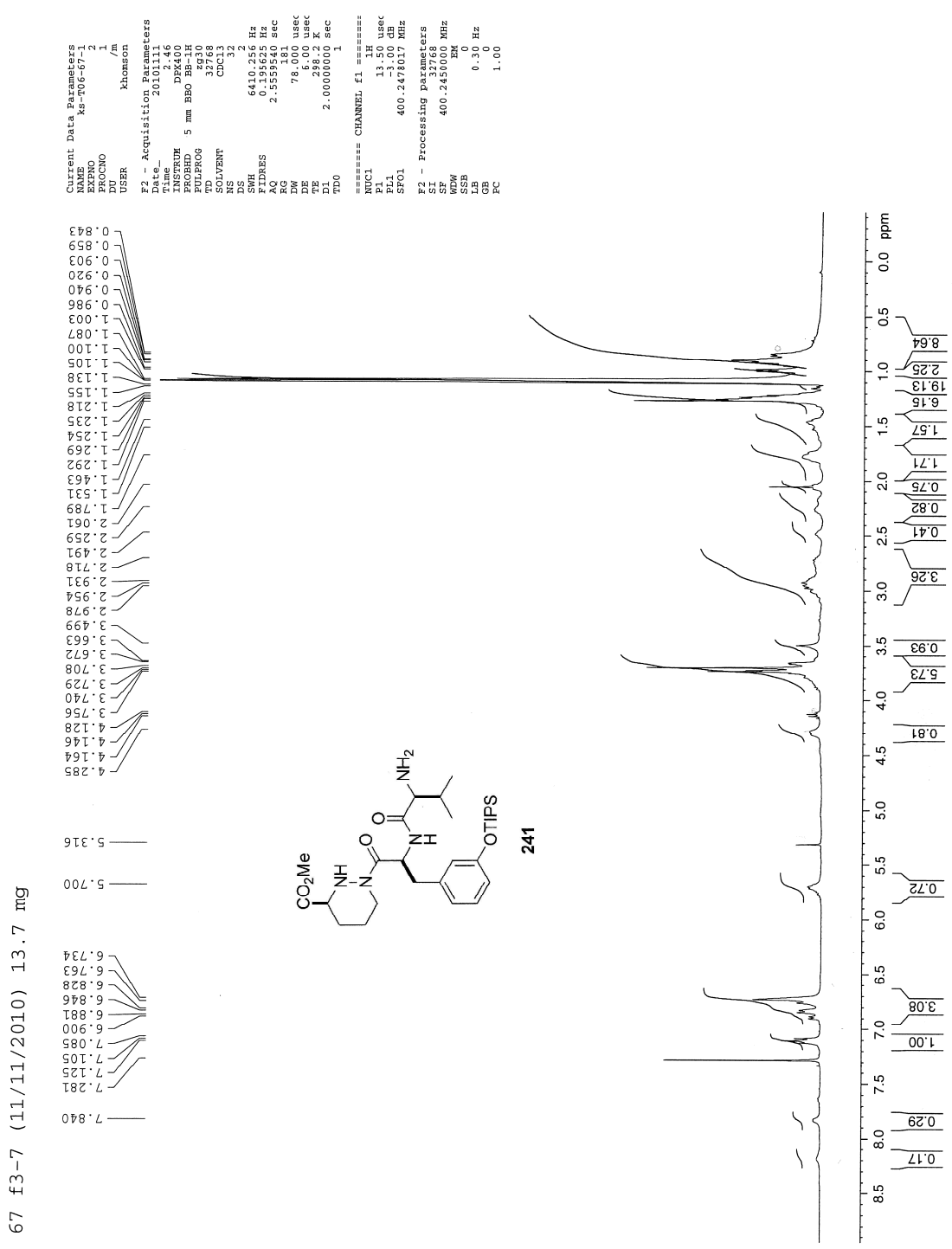

32 f5-16 (2/1/2011) 11.4 mg 13C
NAME 32
EXPNO 2
PROCNO 1
Date_ 20110201
Time 16.24
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 416
DS 4
SWH 41666.668
FIDRES 0.423855
AQ 1.1796980
RG 203
DW 12.000
DE 15.00
TE 298.2
D1 2.00000000
D11 0.03000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 9.00
PL1 4.50
PL1W 38.14553833
SFO1 176.0629186
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00
PL2 -3.20
PL12 13.60
PL13 120.00
PL2W 33.59817505
PL12W 0.70196527
PL13W 0.00000000
SFO2 700.1228005
SI 131072
SF 176.0453140
WDW EM
SSB 0
LB 3.00
GB 0
PC 1.40
339
OTIPS
t-BuO
ppm

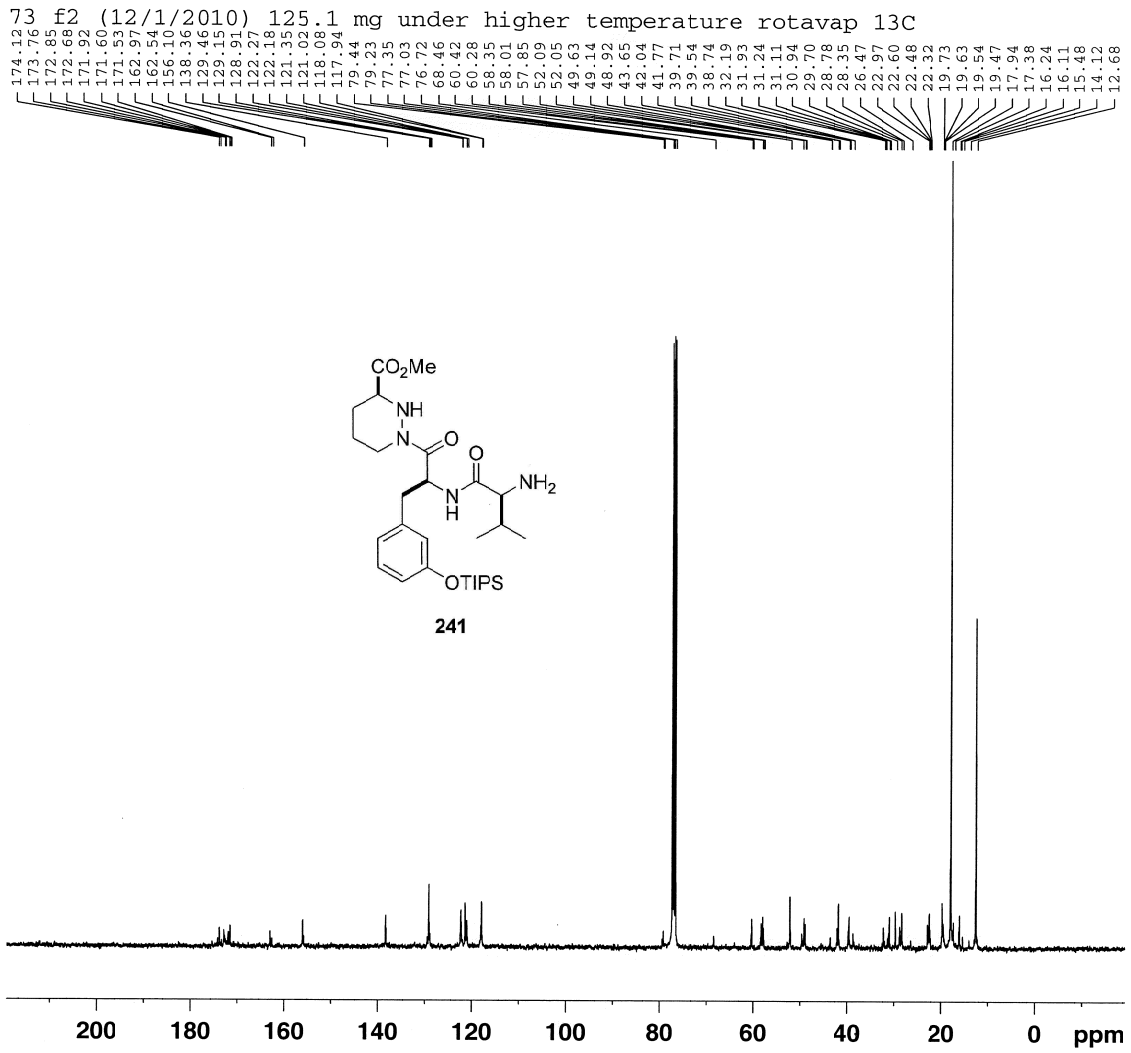

49 f31-55 (10/5/2010) 79.3 mg
Current Data Parameters
NAME ks-T06-49-1
EXPNO 3
PROCNO 1
F2 - Acquisition Parameter
Date_ 20101005
Time 17.26
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 Hz
FIDRES 0.207320 Hz
AQ 2.4117749 se
RG 35.9
DW 73.600 us
DE 6.50 us
TE 298.9 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
SFO1 400.1424008 MH
F2 - Processing parameters
SI 32768
SF 400.1400000 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.355
7.282
7.100
6.760
6.741
5.152
5.123
5.095
5.065
4.834
4.818
4.801
3.151
3.130
3.116
3.062
3.046
1.282
1.249
1.104
1.086
HO
O
O
NH
NHCbz
OTIPS
342
4.78
1.00
2.90
0.96
0.72
1.96
0.94
0.95
1.88
1.57
7.11
18.14
7.88
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


58 f22-30 2nd column (10/28/2010) 612.4 mg 13C
Current Data Parameters
NAME ks-T06-58-1
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101028
Time 1.22
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2278
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 9195.2
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
174.19
171.62
156.54
156.23
137.24
137.02
136.28
129.49
128.52
128.15
128.00
122.12
120.90
118.68
77.44
77.13
76.81
67.09
60.32
53.20
37.41
31.17
19.05
17.94
12.66
HO
O
O
N
H
NHCbz
OTIPS
342
ppm

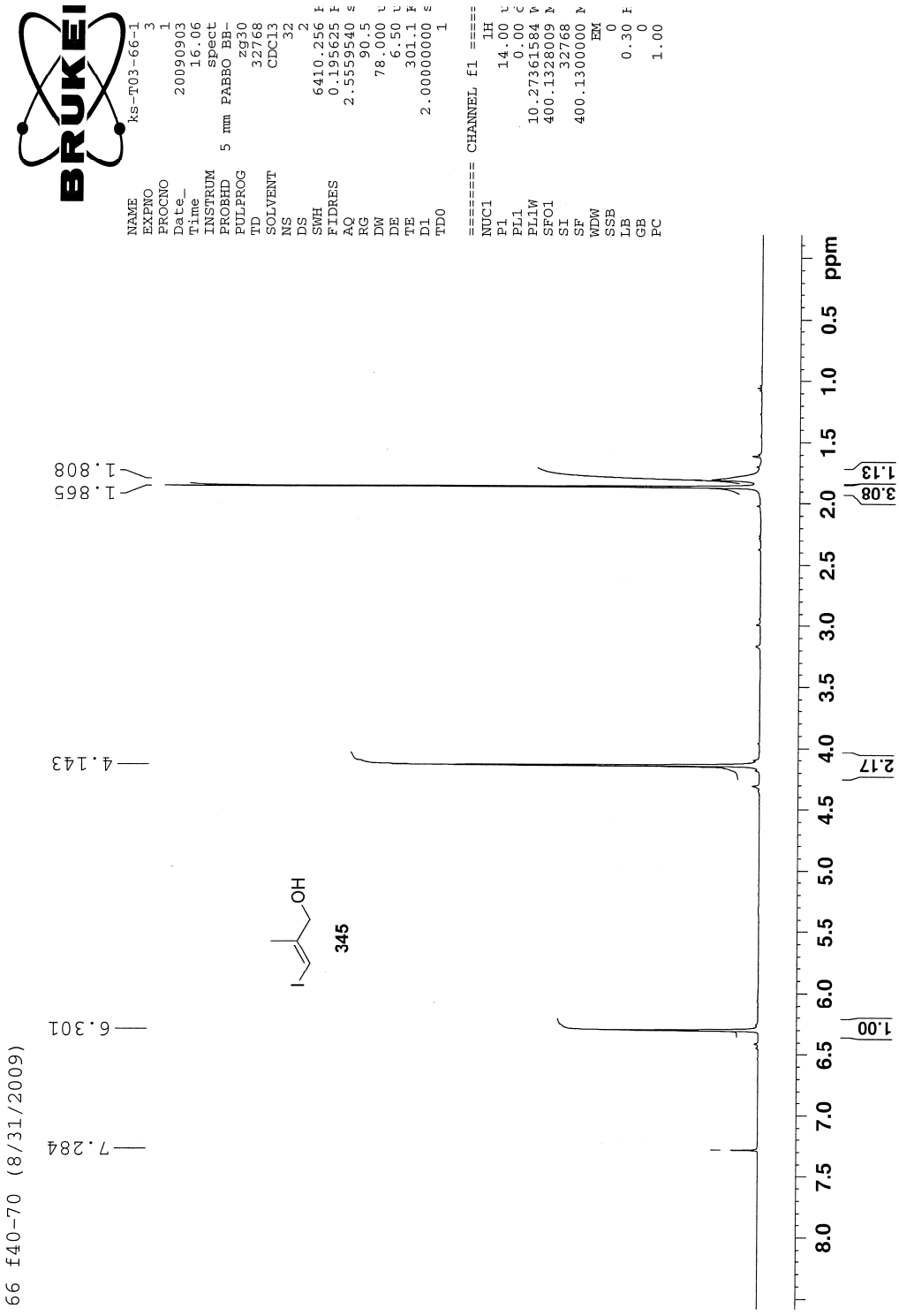

50 f14-24 (10/8/2010) 11.0 mg
Current Data Parameters
NAME ks-T06-50-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20101008
Time_ 14.11
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 Hz
FIDRES 0.207320 Hz
AQ 2.4117749 sec
RG 128
DW 73.600 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1424008 MHz
F2 - Processing parameters
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CO2Me
NH
N
O
O
N
H
NHCbz
OTIPS
343
ppm

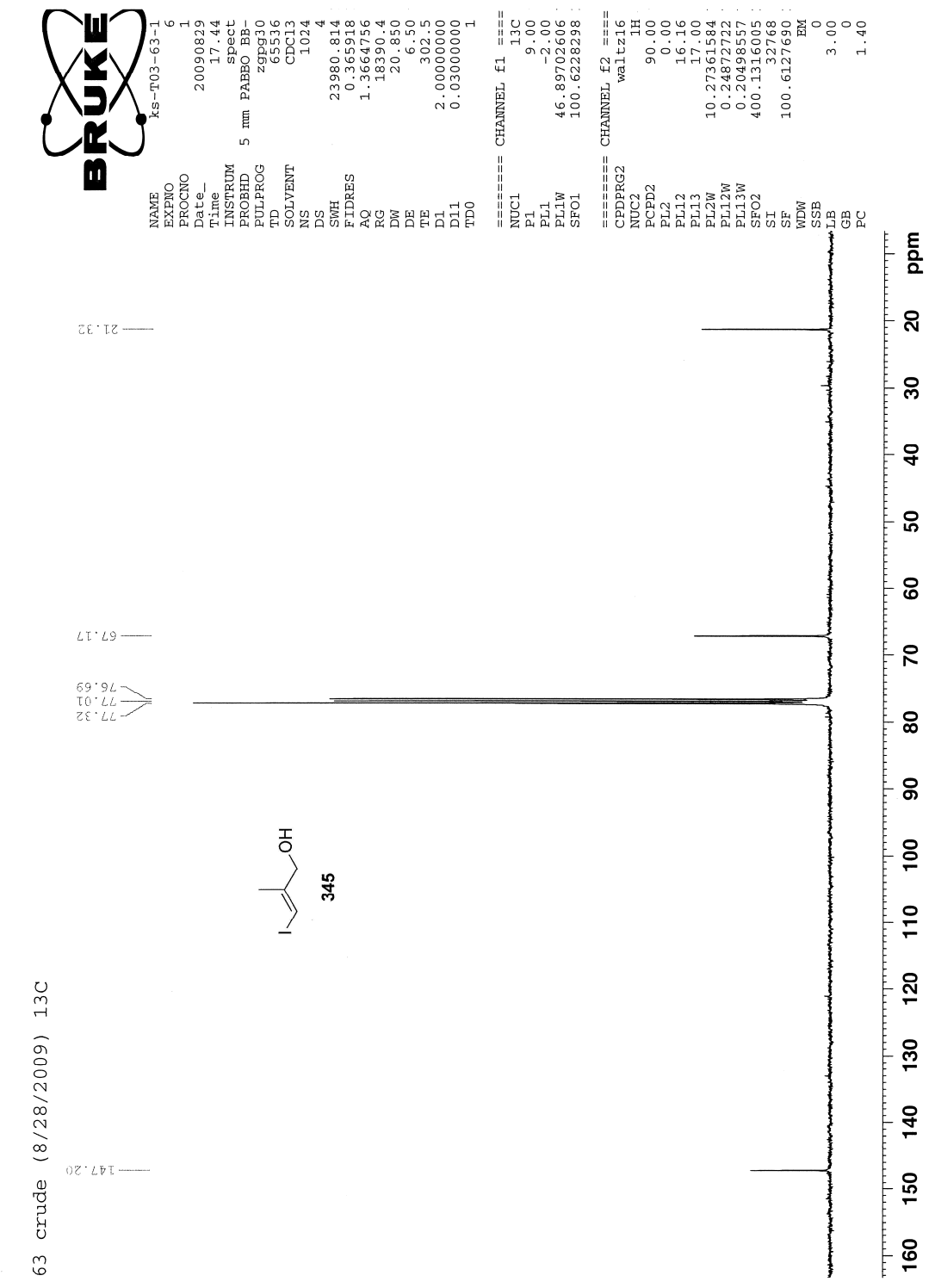

50 f14-24 (10/8/2010) 11.0 mg diels 13C
Current Data Parameters
NAME ks-T06-50-1
EXPNO 6
PROCNO 1
DU /m
USER thomson
F2 - Acquisition Parameters
Date_ 20101008
Time 20.11
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 48933
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 9195.2
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
77.34
77.03
76.71
66.98
60.20
59.98
58.42
57.67
52.11
50.00
49.71
42.00
41.85
39.54
39.08
31.66
31.43
29.71
28.65
28.20
22.89
22.42
19.21
17.94
17.53
17.30
12.68
137.95
136.39
129.19
129.13
128.52
128.09
122.40
122.17
121.35
121.02
118.14
172.29
171.73
171.46
170.35
170.24
156.27
156.14
156.03
CO2Me
NH
N
N
O
O
H
N
NHCbz
OTIPS
343
ppm

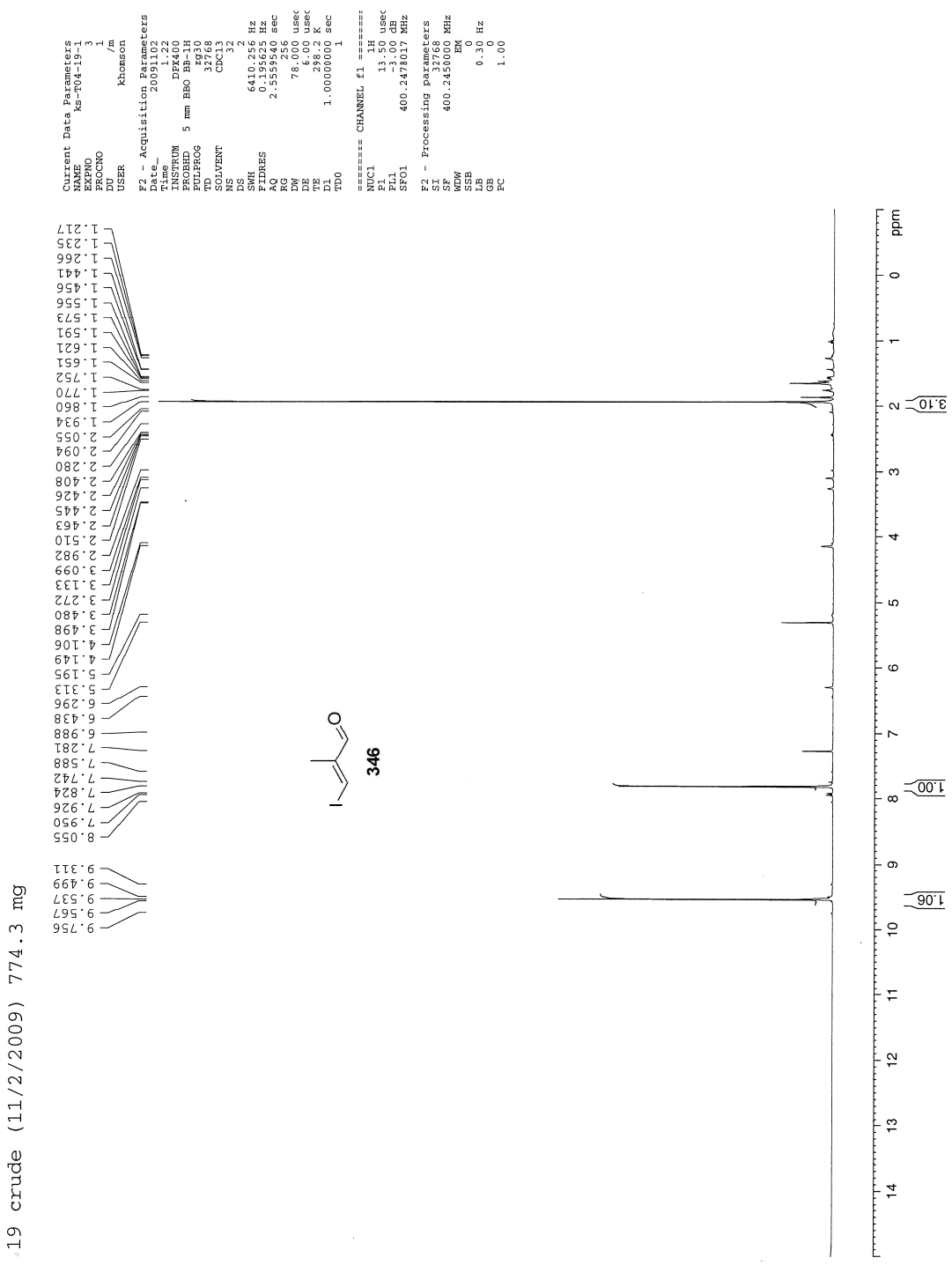

67 f3-7 (11/11/2010) 13.7 mg
Current Data Parameters
NAME ks-T06-67-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20101111
Time 21.46
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
241
ppm

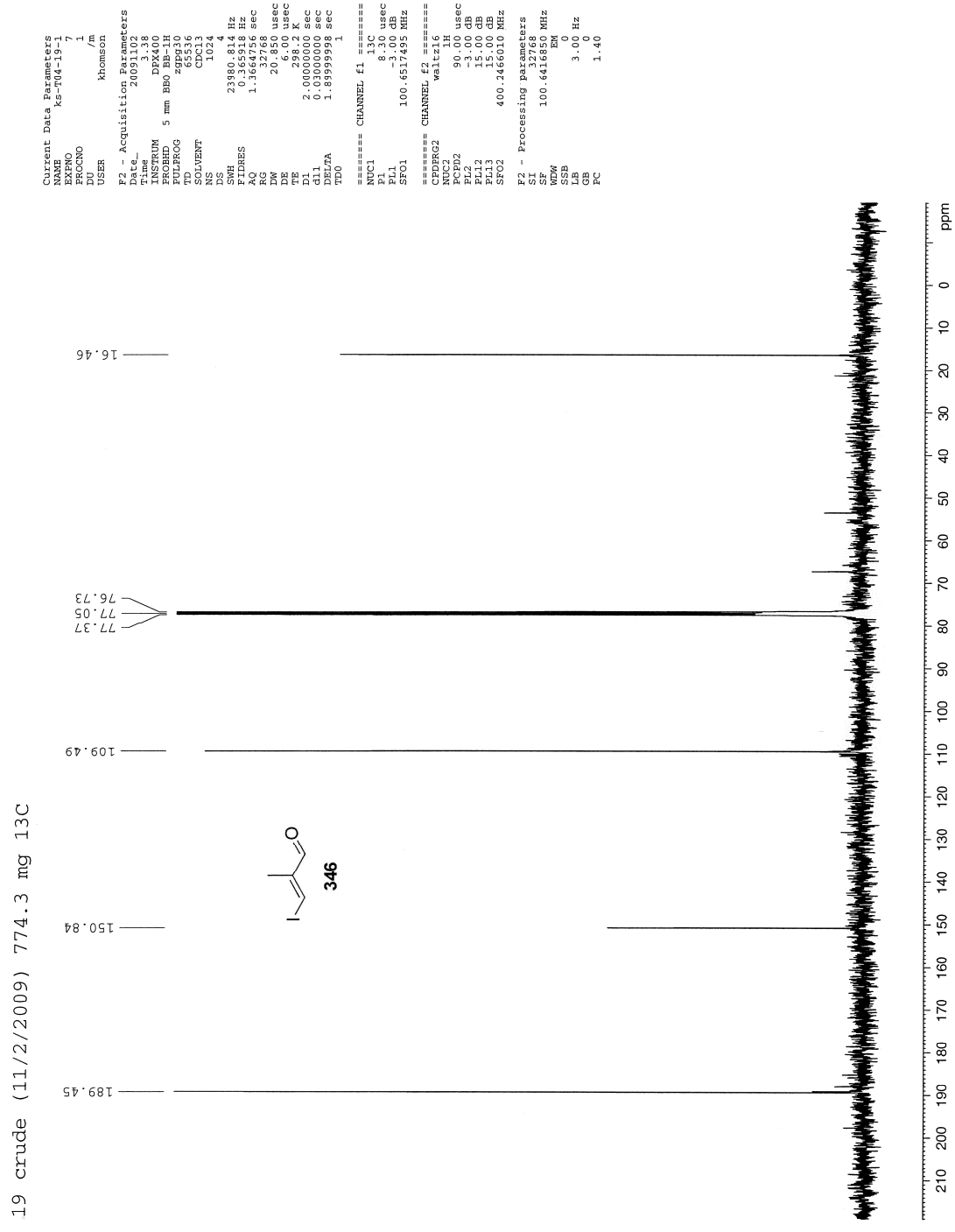


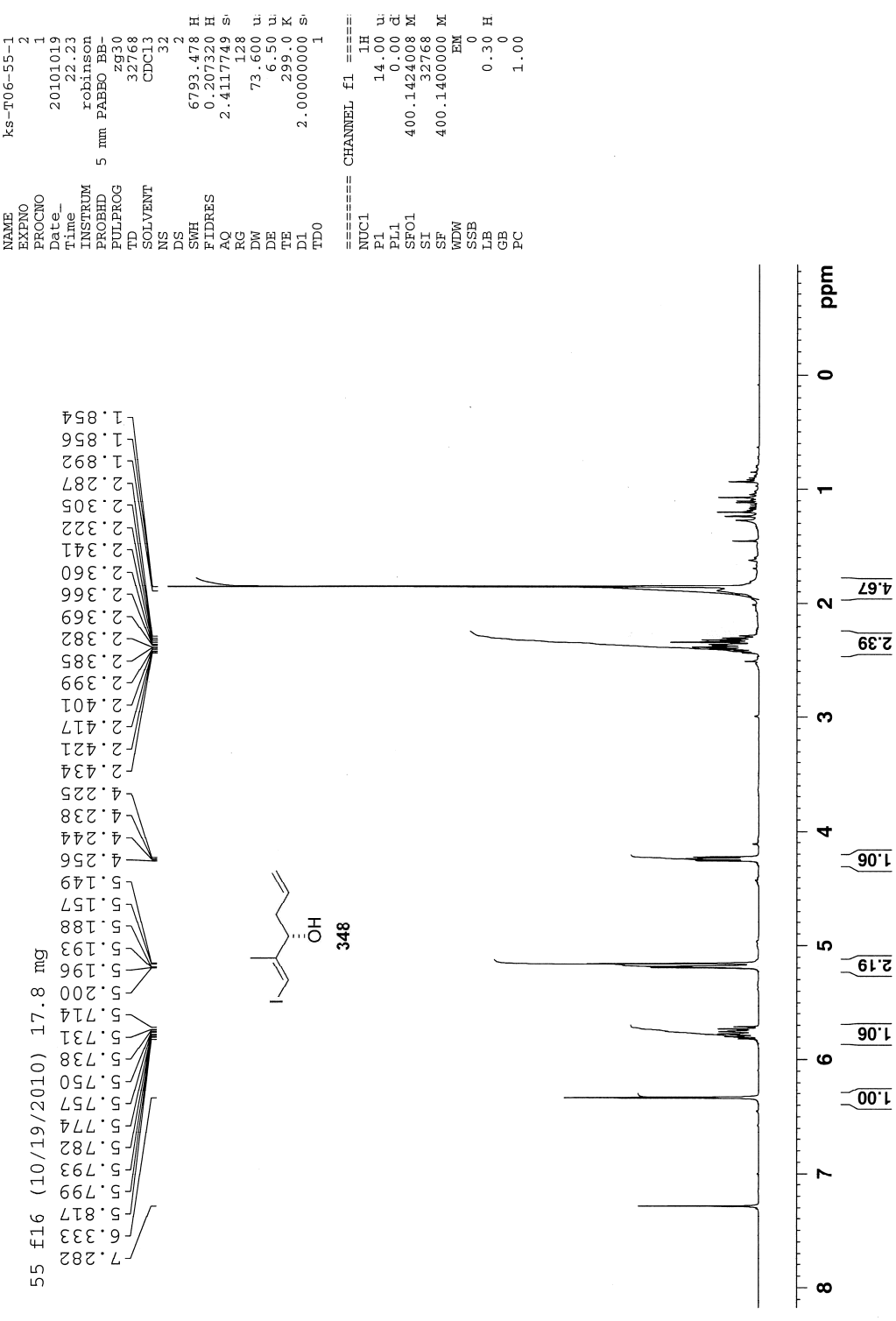

```
Current Data Parameters
NAME          ks-T06-73-1
EXPNO                   4
PROCNO                  1

F2 - Acquisition Parameters
Date_           20101201
Time                6.10
INSTRUM          DPX400
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 6566
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664756 sec
RG                 6502
DW               20.850 usec
DE                6.00 usec
TE                298.2 K
D1           0.20000000 sec
d11          0.03000000 sec
DELTA        0.10000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                  8.30 usec
PL1                -3.00 dB
SFO1        100.6517495 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             90.00 usec
PL2               -3.00 dB
PL12              15.00 dB
PL13              15.00 dB
SFO2        400.2466010 MHz

F2 - Processing parameters
SI                32768
SF          100.6416850 MHz
WDW                  EM
SSB                   0
LB                 3.00 Hz
GB                    0
PC                 1.00
```

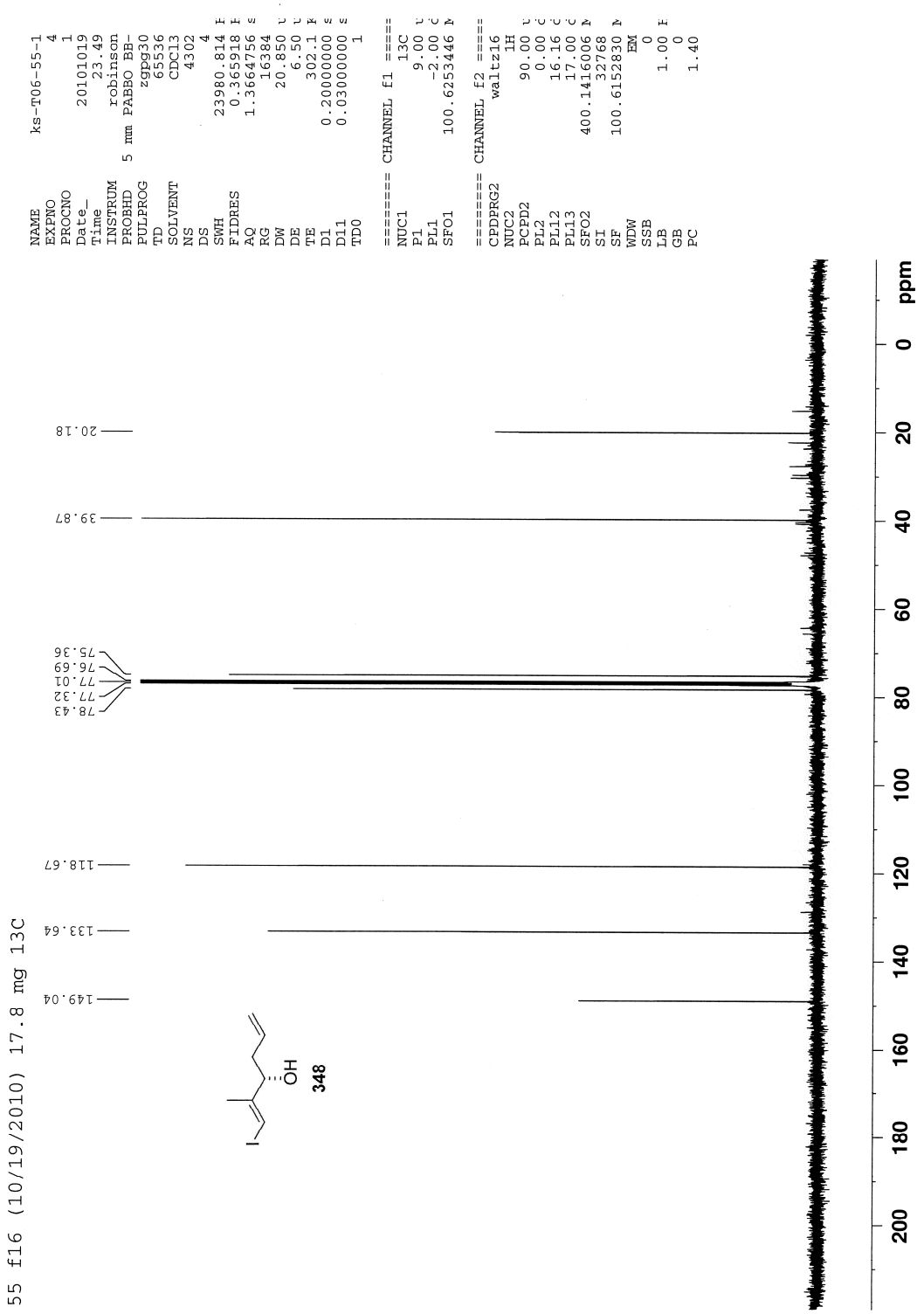

66 f40-70 (8/31/2009)
7.284
6.301
4.143
1.865
1.808
345
1.00
2.17
3.08
1.13
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
NAME ks-T03-66-1
EXPNO 3
PROCNO 1
Date_ 20090903
Time_ 16.06
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 90.5
DW 78.000 u
DE 6.50 u
TE 301.1 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1328009 M
SI 32768
SF 400.1300000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00

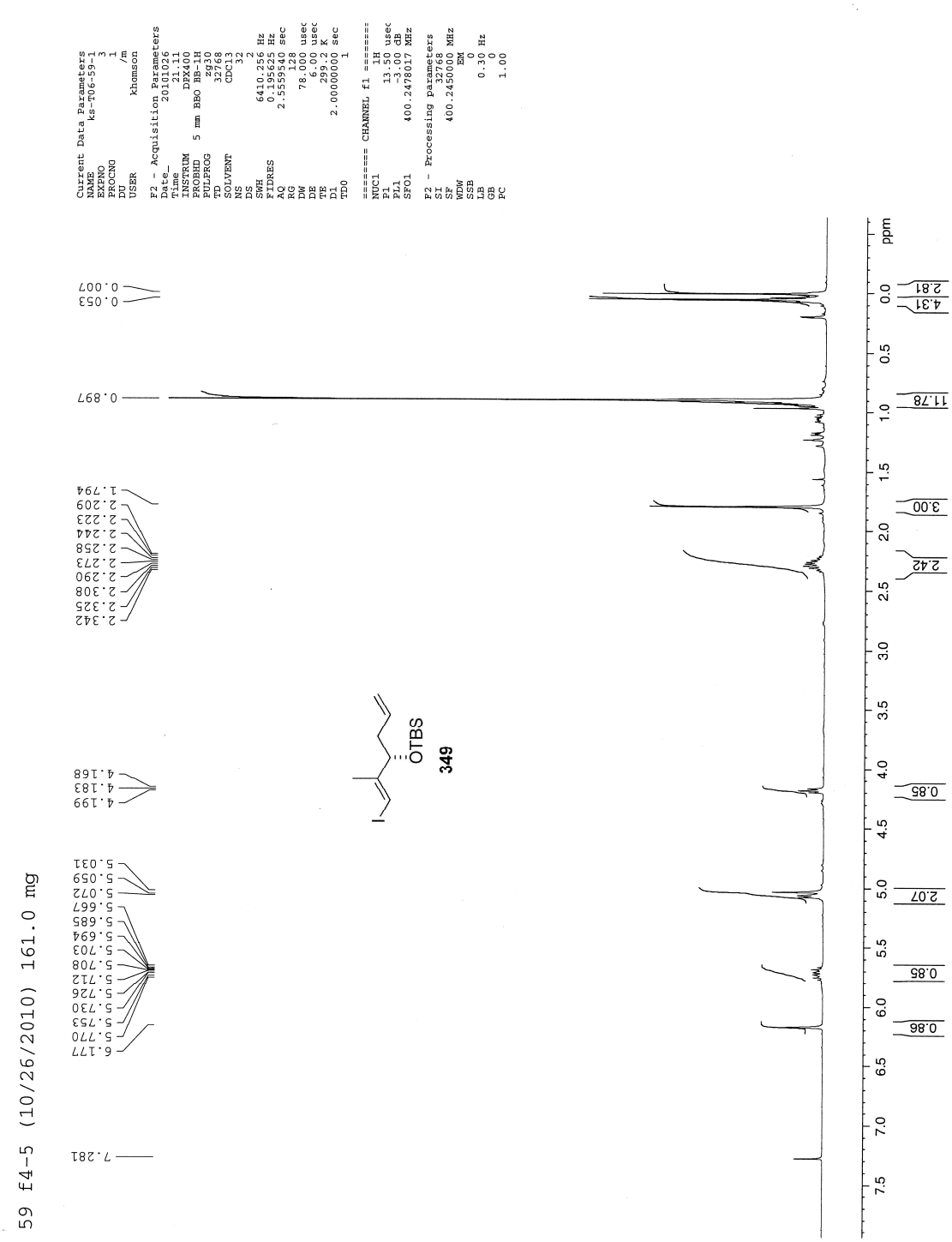

63 crude (8/28/2009) 13C
345
147.20
77.32
77.01
76.69
67.17
21.32
ppm
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
NAME Ks-T03-63-1
EXPNO 6
PROCNO 1
Date_ 20090829
Time 17.44
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814
FIDRES 0.365918
AQ 1.3664756
RG 18390.4
DW 20.850
DE 6.50
TE 302.5
D1 2.00000000
D11 0.03000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 9.00
PL1 -2.00
PL1W 46.89702606
SFO1 100.6228298
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00
PL2 0.00
PL12 16.16
PL13 17.00
PL2W 10.27361584
PL12W 0.24872722
PL13W 0.20498557
SFO2 400.1316005
SI 32768
SF 100.6127690
WDW EM
SSB 0
LB 3.00
GB 0
PC 1.40

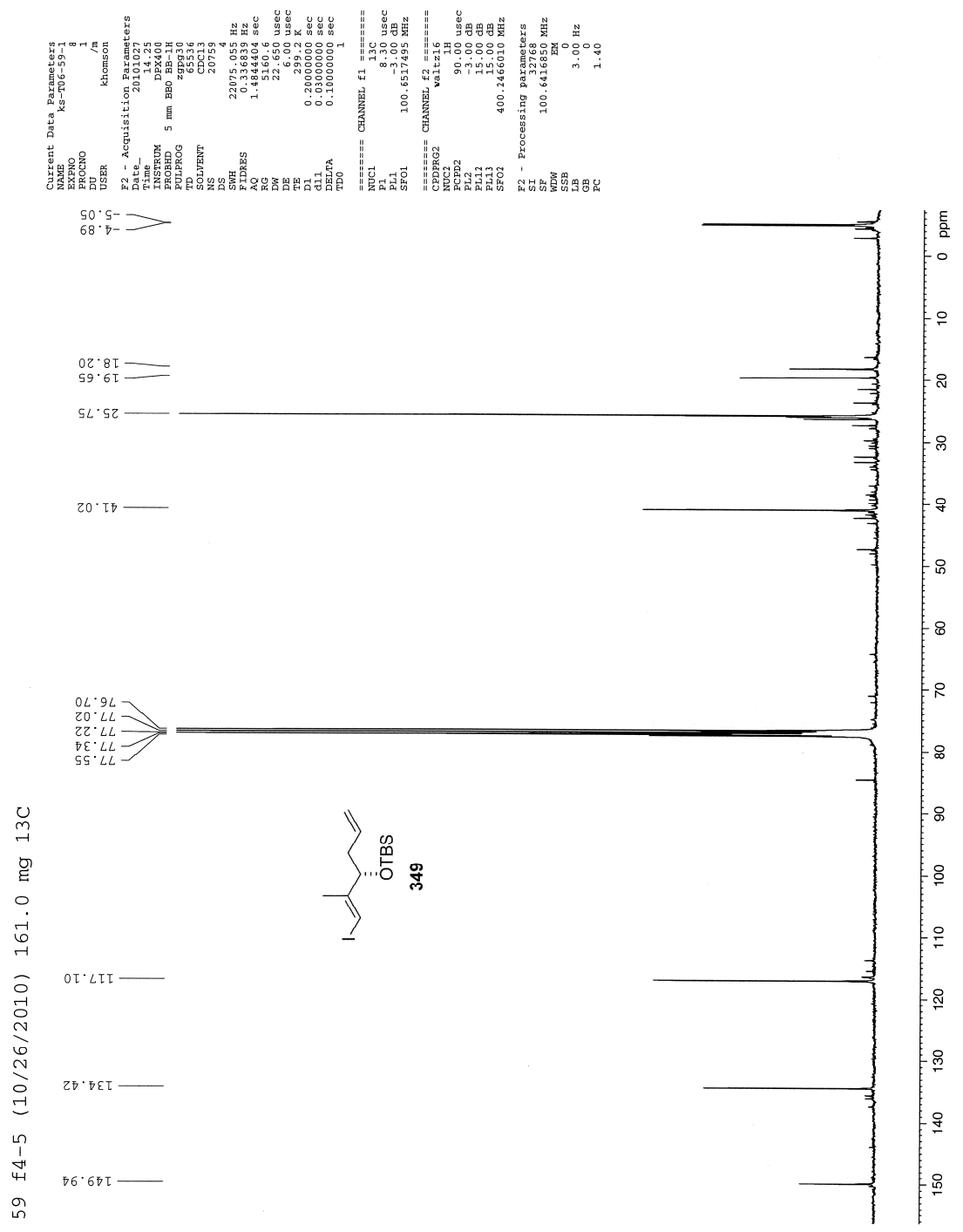

19 crude (11/2/2009) 774.3 mg
Current Data Parameters
NAME ks-t04-19-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091102
Time 12
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 256
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
346
3.10
1.00
1.06
ppm

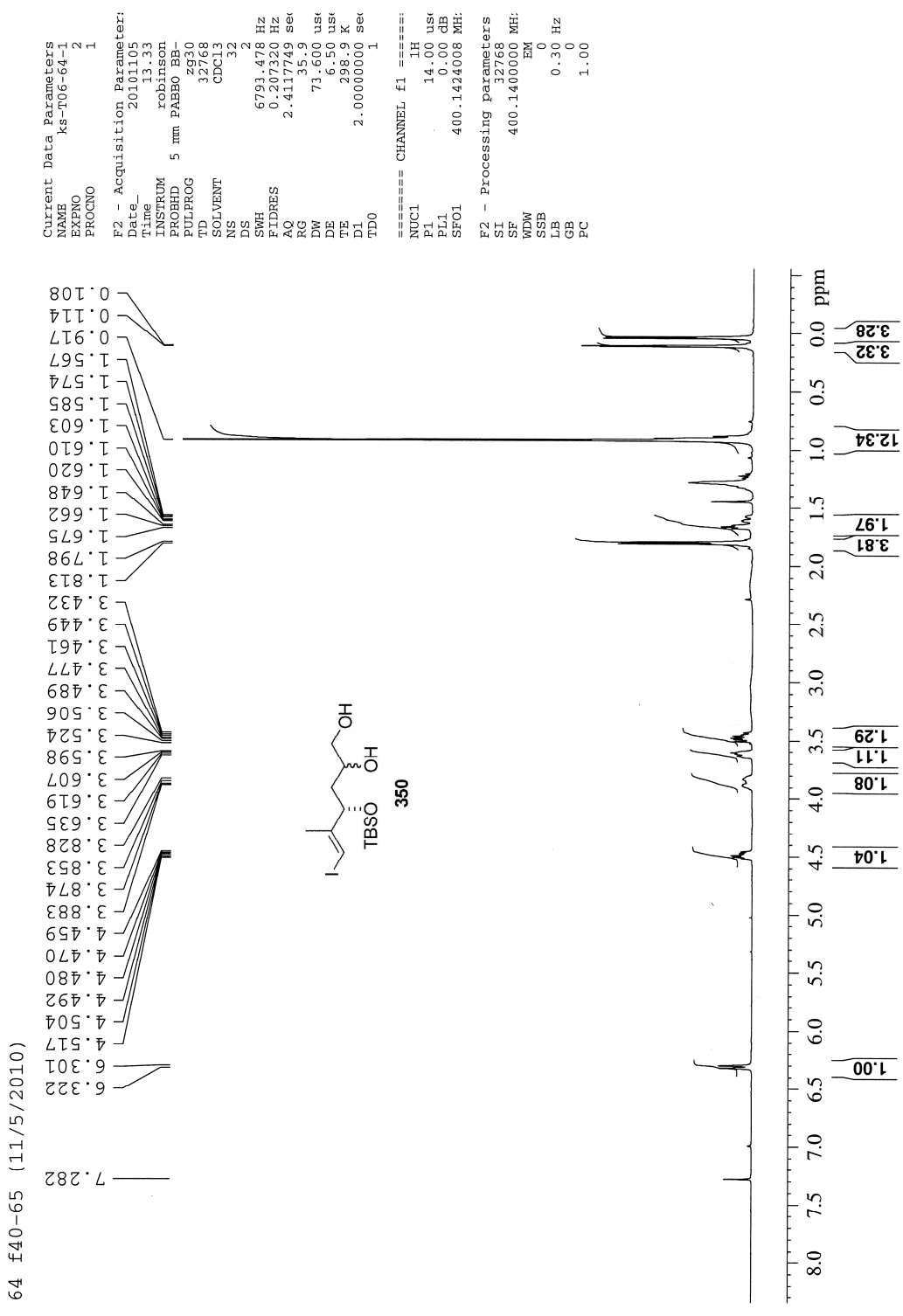

19 crude (11/2/2009) 774.3 mg 13C
Current Data Parameters
NAME ks-T04-19-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091102
Time 3.38
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.36664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
189.45
150.84
109.49
77.37
77.05
76.73
16.46
346
ppm

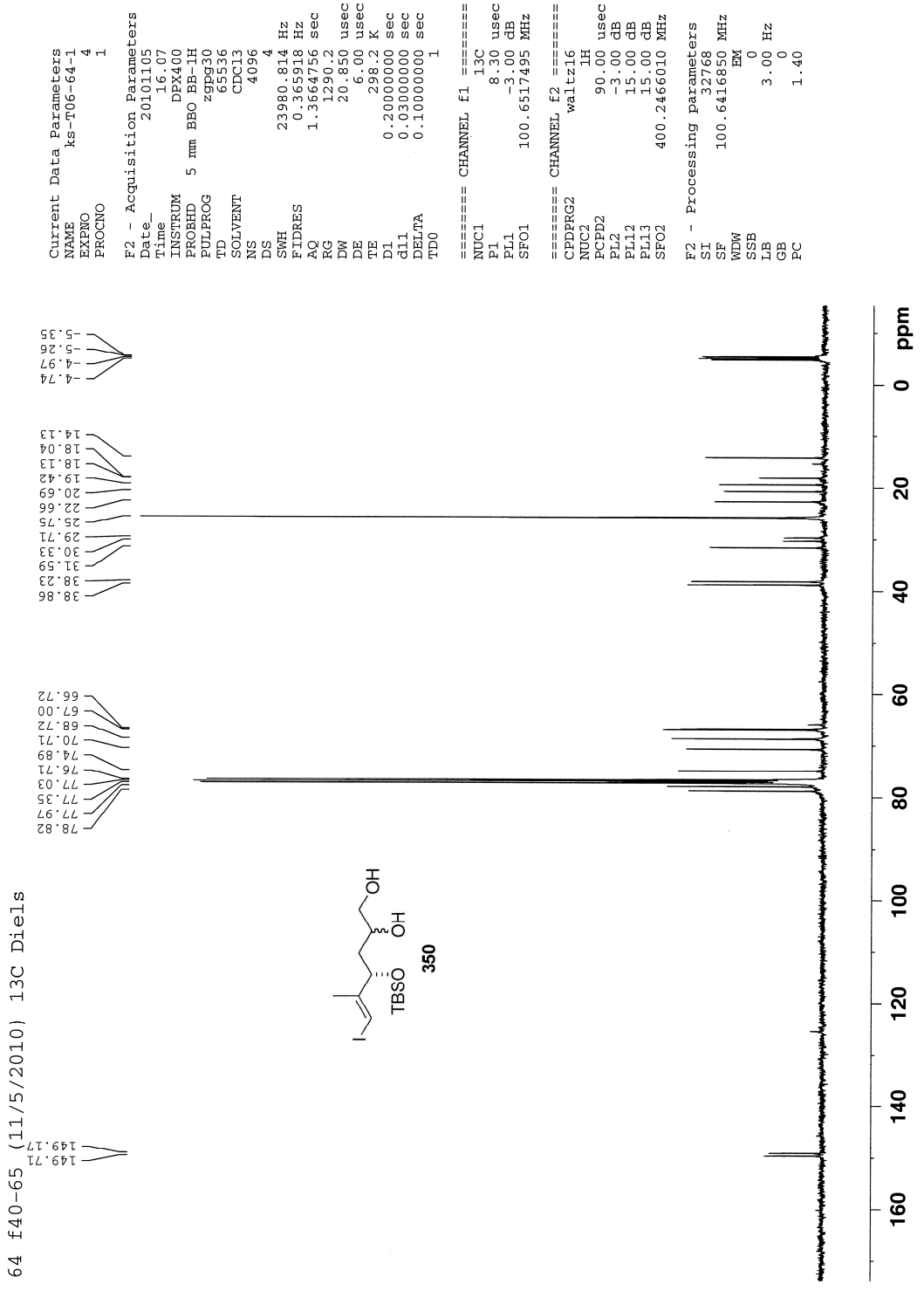

NAME ks-T06-55-1
EXPNO 2
PROCNO 1
Date_ 20101019
Time 22.23
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 128
DW 73.600 u
DE 6.50 u
TE 299.0 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
55 f16 (10/19/2010) 17.8 mg
7.282
6.333
5.817
5.799
5.793
5.782
5.774
5.757
5.750
5.738
5.731
5.714
5.200
5.196
5.193
5.188
5.157
5.149
4.256
4.244
4.238
4.225
2.434
2.421
2.417
2.401
2.399
2.385
2.382
2.369
2.366
2.360
2.341
2.322
2.305
2.287
1.892
1.856
1.854
348
OH
I
ppm
8
7
6
5
4
3
2
1
0
1.00
1.06
2.19
1.06
2.39
4.67

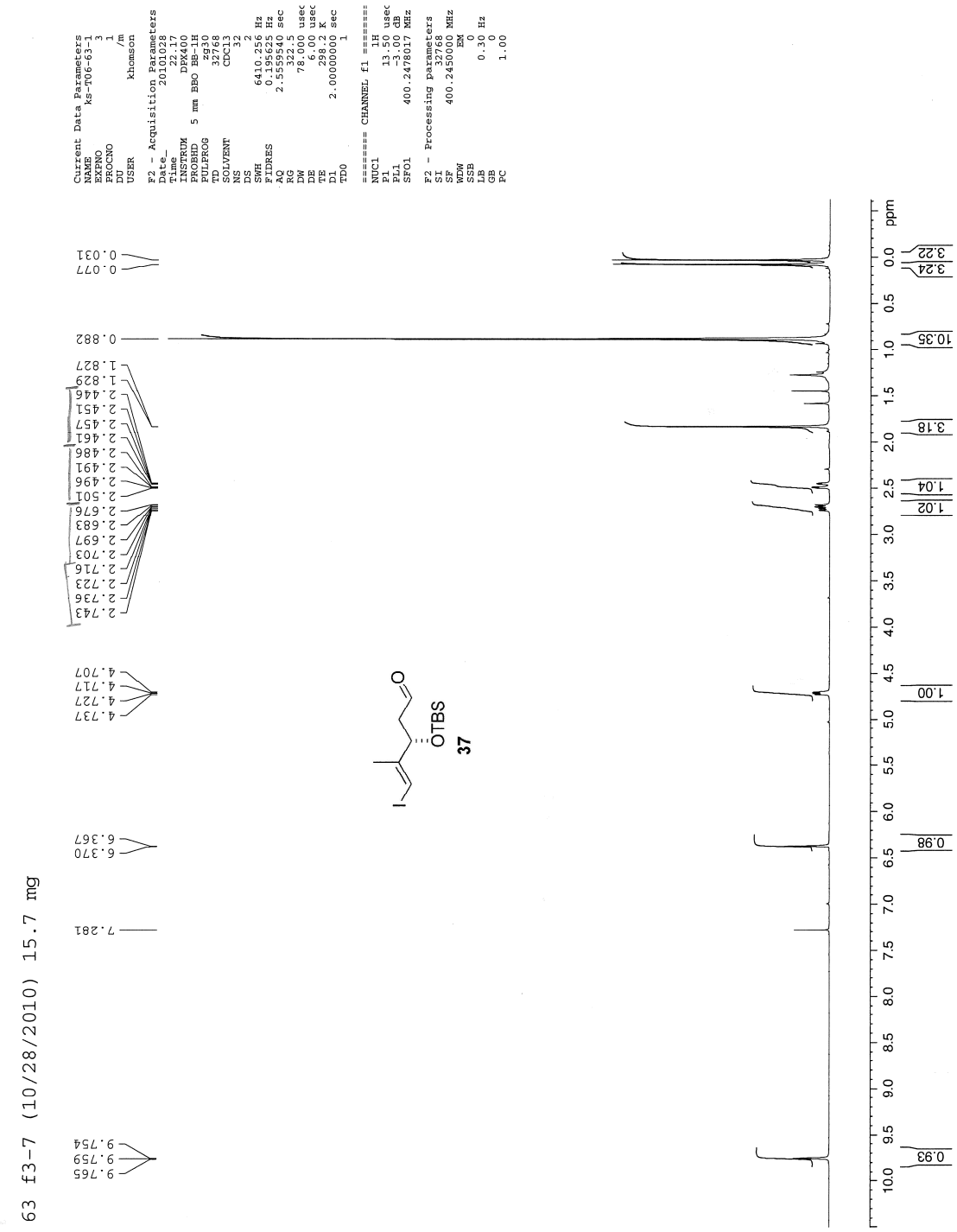

55 f16 (10/19/2010) 17.8 mg 13C
348
20.18
39.87
75.36
76.69
77.01
77.32
78.43
118.67
133.64
149.04
ppm
0
20
40
60
80
100
120
140
160
180
200

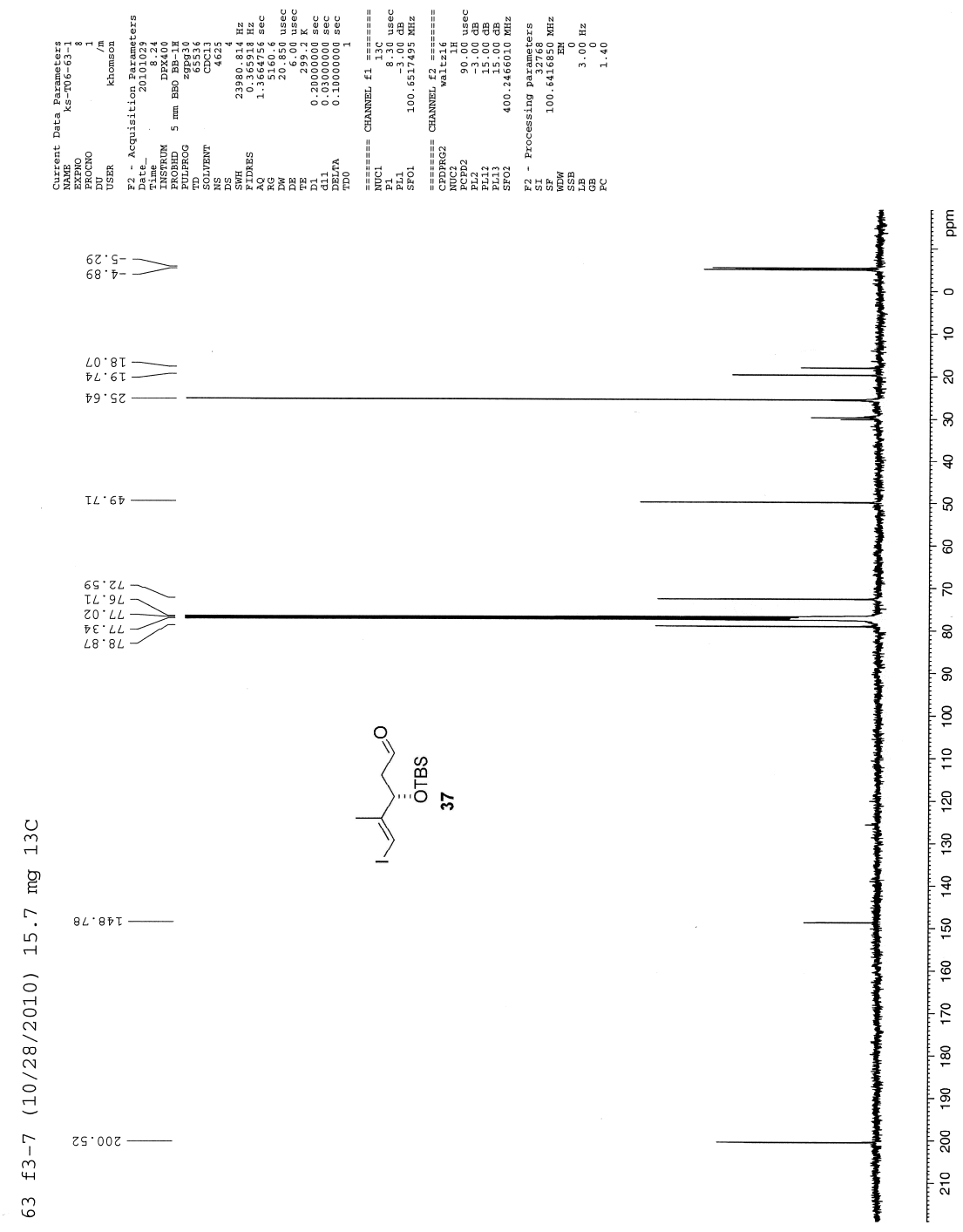

59 f4-5 (10/26/2010) 161.0 mg
Current Data Parameters
NAME ks-706-59-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20101026
Time_ 21.11
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 128
DW 78.000 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTBS
349
ppm

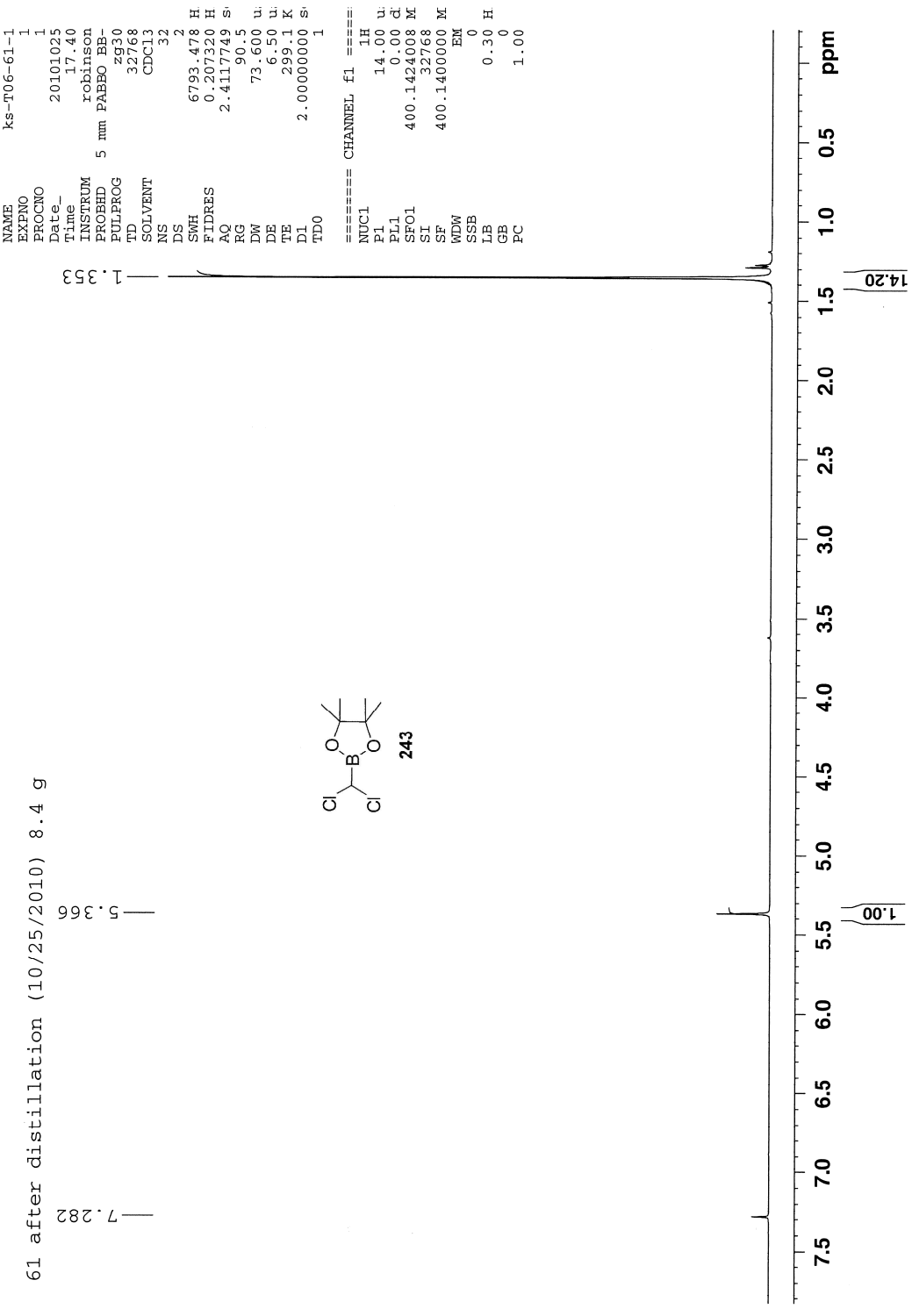

59 f4-5 (10/26/2010) 161.0 mg 13C
Current Data Parameters
NAME ks-T06-59-1
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101027
Time 14.25
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 20759
DS 4
SWH 22075.055 Hz
FIDRES 0.336839 Hz
AQ 1.4844404 sec
RG 5160.6
DW 22.650 usec
DE 6.00 usec
TE 299.2 K
D1 0.20000000 sec
D11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416650 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
149.94
134.42
117.10
77.55
77.34
77.22
77.02
76.70
41.02
25.75
19.65
18.20
-4.89
-5.05
OTBS
349
0 ppm

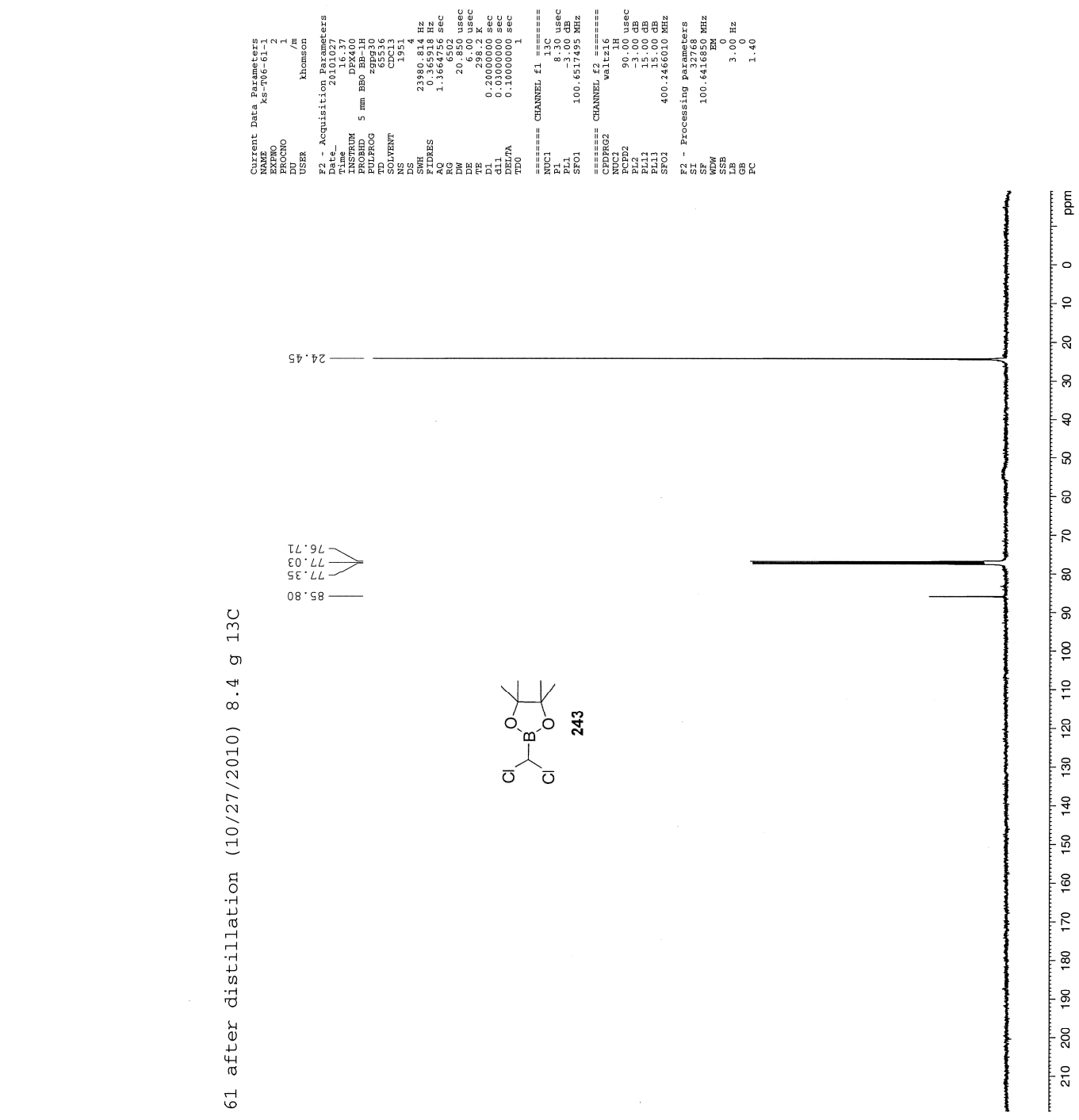

64 f40-65 (11/5/2010)
Current Data Parameters
NAME ks-T06-64-1
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20101105
Time_ 13.33
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 Hz
FIDRES 0.207320 Hz
AQ 2.4117749 se
RG 35.9
DW 73.600 us
DE 6.50 us
TE 298.9 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
SFO1 400.1424008 MH
F2 - Processing parameters
SI 32768
SF 400.1400000 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.282
6.322
6.301
4.517
4.504
4.492
4.480
4.470
4.459
3.883
3.874
3.853
3.828
3.635
3.619
3.607
3.598
3.524
3.506
3.489
3.477
3.461
3.449
3.432
1.813
1.798
1.675
1.662
1.648
1.620
1.610
1.603
1.585
1.574
1.567
0.917
0.114
0.108
OH
OH
TBSO
I
350
1.00
1.04
1.08
1.11
1.29
3.81
1.97
12.34
3.32
3.28
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

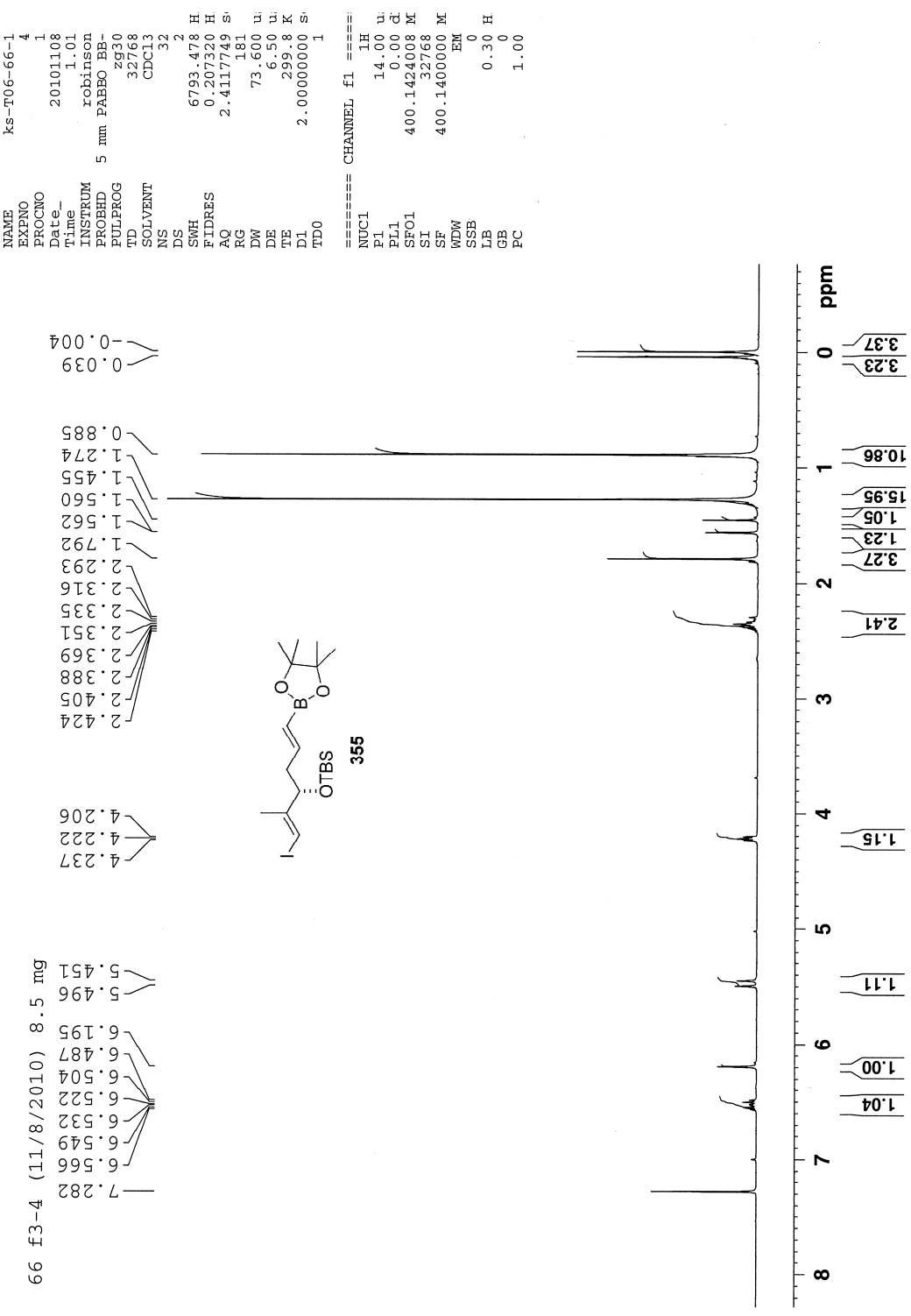

64 f40-65 (11/5/2010) 13C Diels
Current Data Parameters
NAME ks-T06-64-1
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101105
Time 16.07
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4096
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 1290.2
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
149.71
149.17
78.82
77.97
77.35
77.03
76.71
74.89
70.71
68.72
67.00
66.72
38.86
38.23
31.59
30.33
29.71
25.75
22.66
20.69
19.42
18.13
18.04
14.13
-4.74
-4.97
-5.26
-5.35
OH
OH
TBSO
I
350
160
140
120
100
80
60
40
20
0
ppm

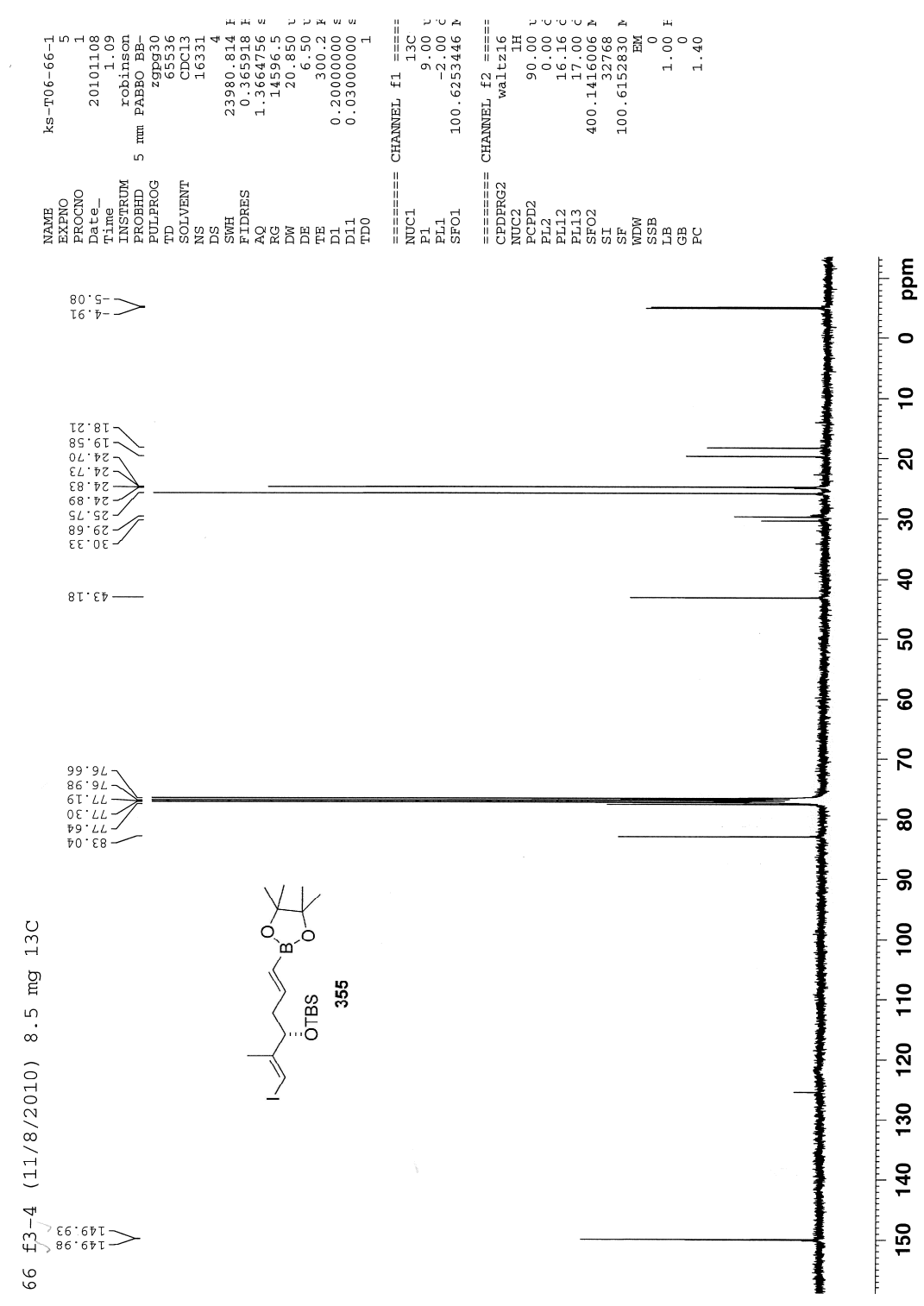

63 f3-7 (10/28/2010) 15.7 mg
Current Data Parameters
NAME ks-T06-63-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20101028
Time 22.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 322.5
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -1.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9.765
9.759
9.754
7.281
6.370
6.367
4.737
4.727
4.717
4.707
2.743
2.736
2.723
2.716
2.703
2.697
2.683
2.676
2.501
2.496
2.491
2.486
2.461
2.457
2.451
2.446
1.829
1.827
0.882
0.077
0.031
OTBS
37
I
O
ppm
0.93
0.98
1.00
1.02
1.04
3.18
10.35
3.24
3.22

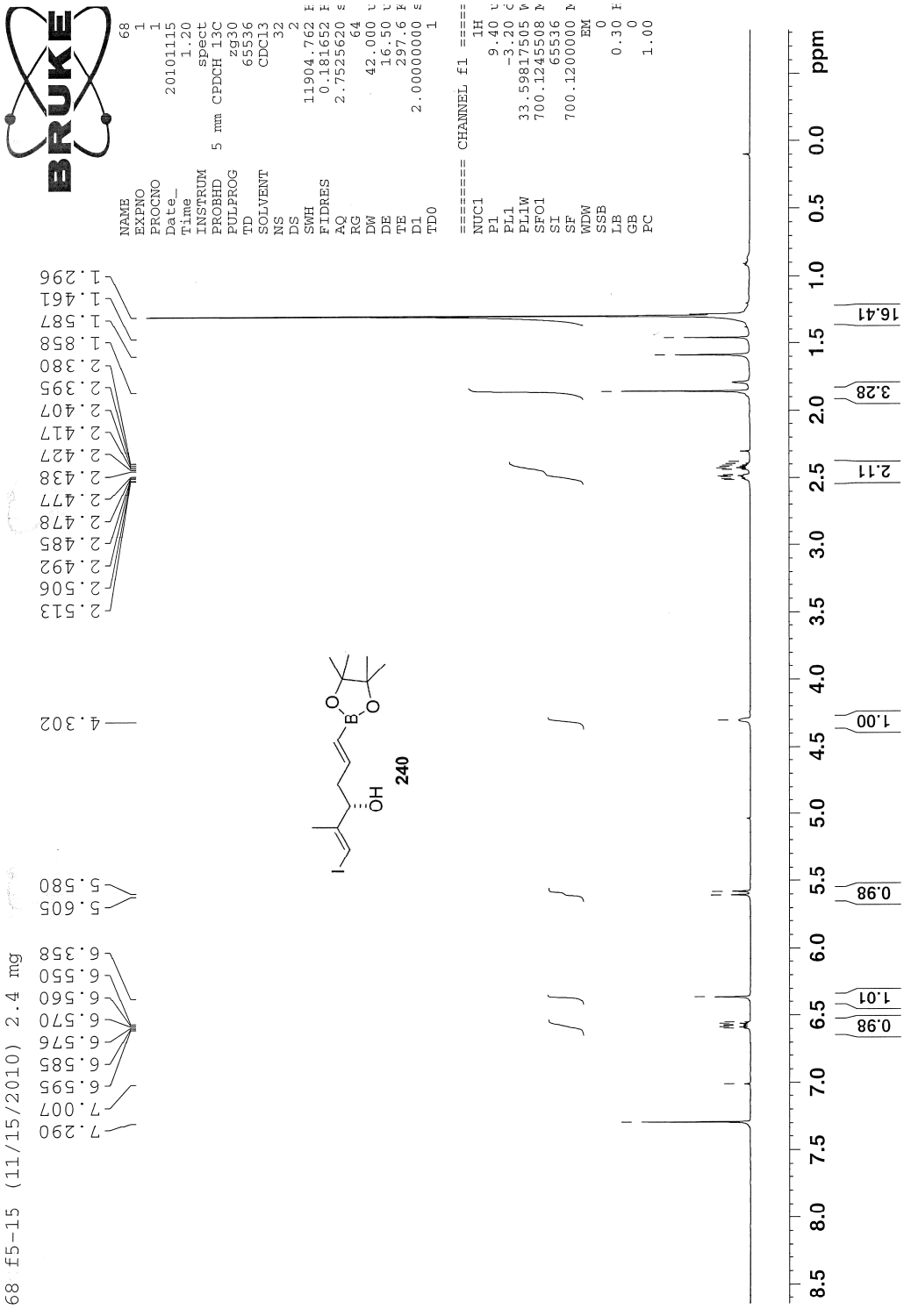

63 f3-7 (10/28/2010) 15.7 mg 13C
Current Data Parameters
NAME ks-706-63-1
EXPNO 8
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20101029
TIME 8.24
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4625
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664755 sec
RG 5160.6
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 0.20000000 sec
d11 0.03000000 sec
PRECPA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
-5.29
-4.89
18.07
19.74
25.64
49.71
72.59
76.71
77.02
77.34
78.87
148.78
200.52
OTBS
37
ppm

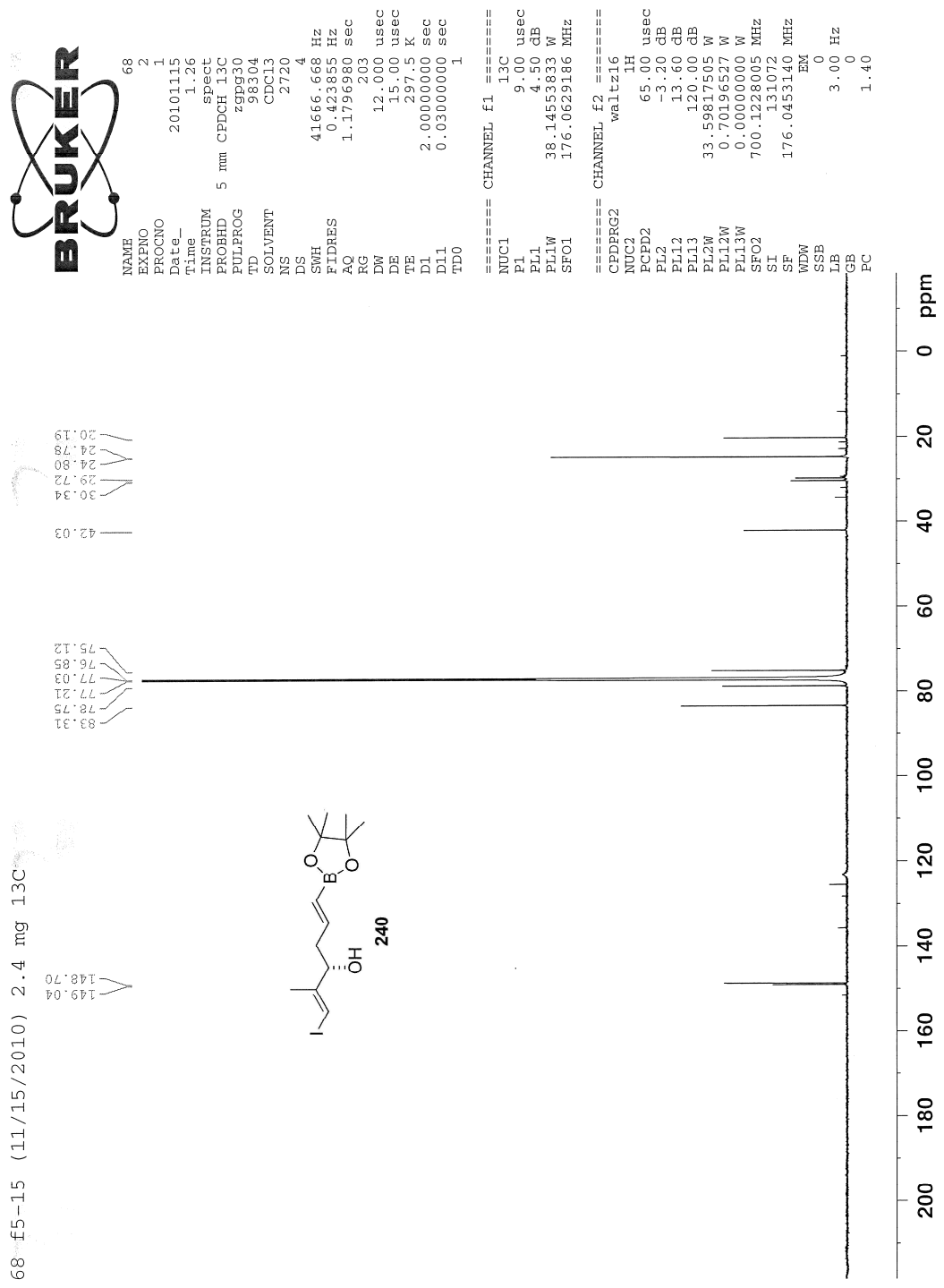

61 after distillation (10/25/2010) 8.4 g
7.282
5.366
1.353
243
14.20
1.00
ppm
NAME ks-T06-61-1
EXPNO 1
PROCNO 1
Date_ 20101025
Time 17.40
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 90.5
DW 73.600 u
DE 6.50 u
TE 299.1 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00

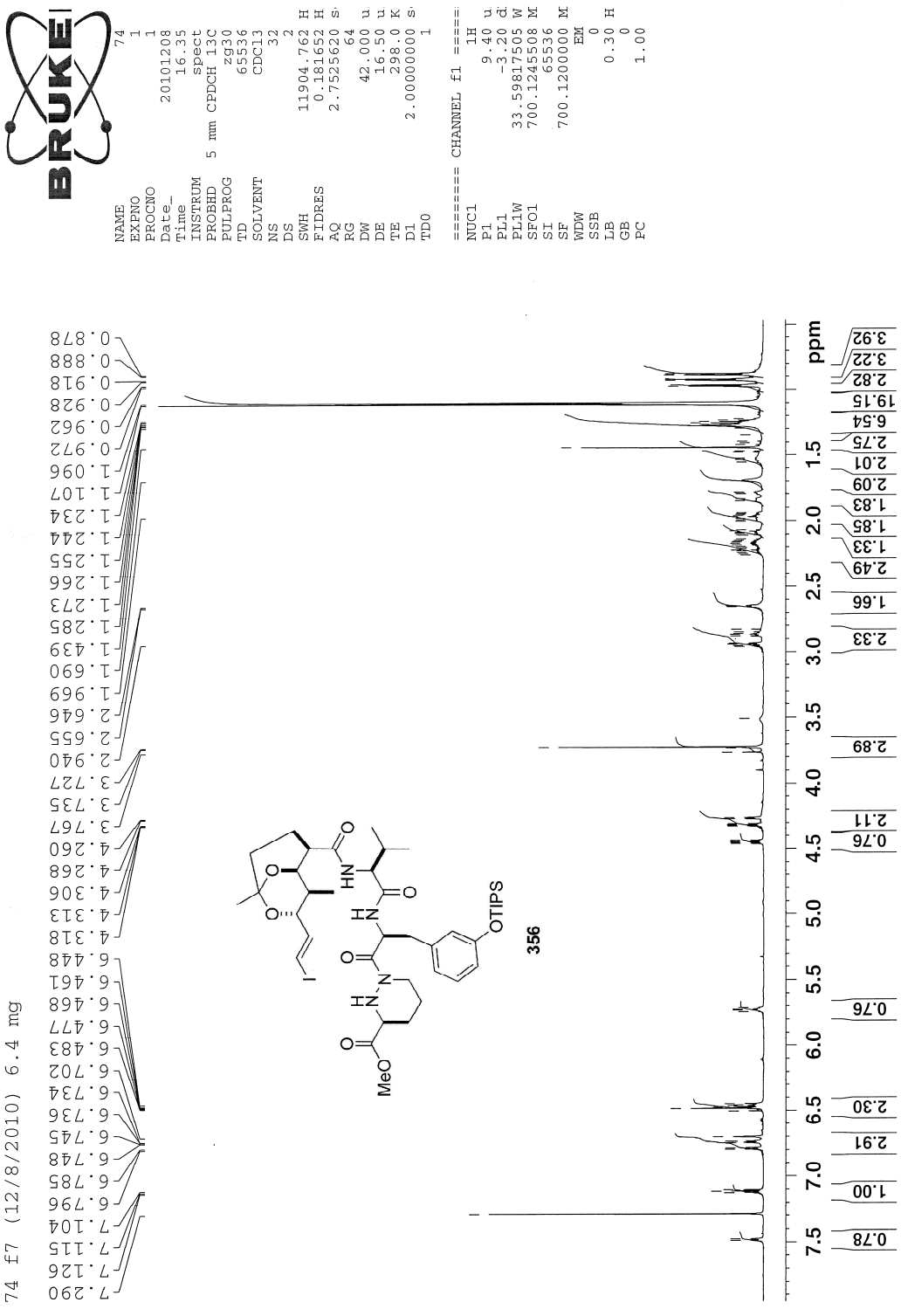

61 after distillation (10/27/2010) 8.4 g 13C
Current Data Parameters
NAME ks-YO6-61-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20101027
Time 16.37
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1951
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 6502
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
24.45
76.71
77.03
77.35
85.80
O
B
O
Cl
Cl
243
ppm

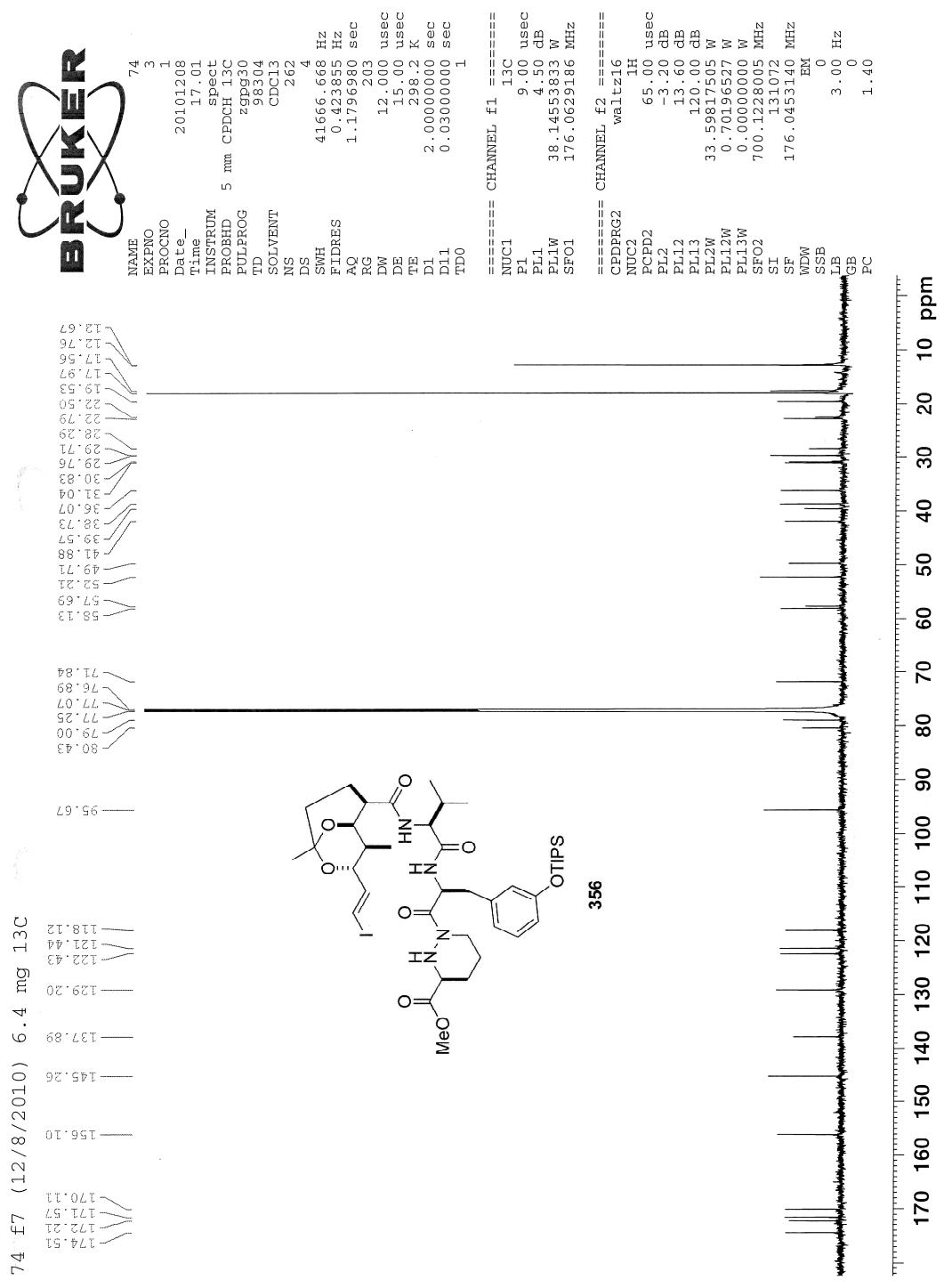

NAME ks-T06-66-1
EXPNO 4
PROCNO 1
Date_ 20101108
Time 1.01
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 181
DW 73.600 u
DE 6.50 u
TE 299.8 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
66 f3-4 (11/8/2010) 8.5 mg
7.282
6.566
6.549
6.532
6.522
6.504
6.487
6.195
5.496
5.451
4.237
4.222
4.206
2.424
2.405
2.388
2.369
2.351
2.335
2.316
2.293
1.792
1.562
1.560
1.455
1.274
0.885
0.039
-0.004
OTBS
355
ppm
0
1
2
3
4
5
6
7
8
3.37
3.23
10.86
15.95
1.05
1.23
3.27
2.41
1.15
1.11
1.00
1.04

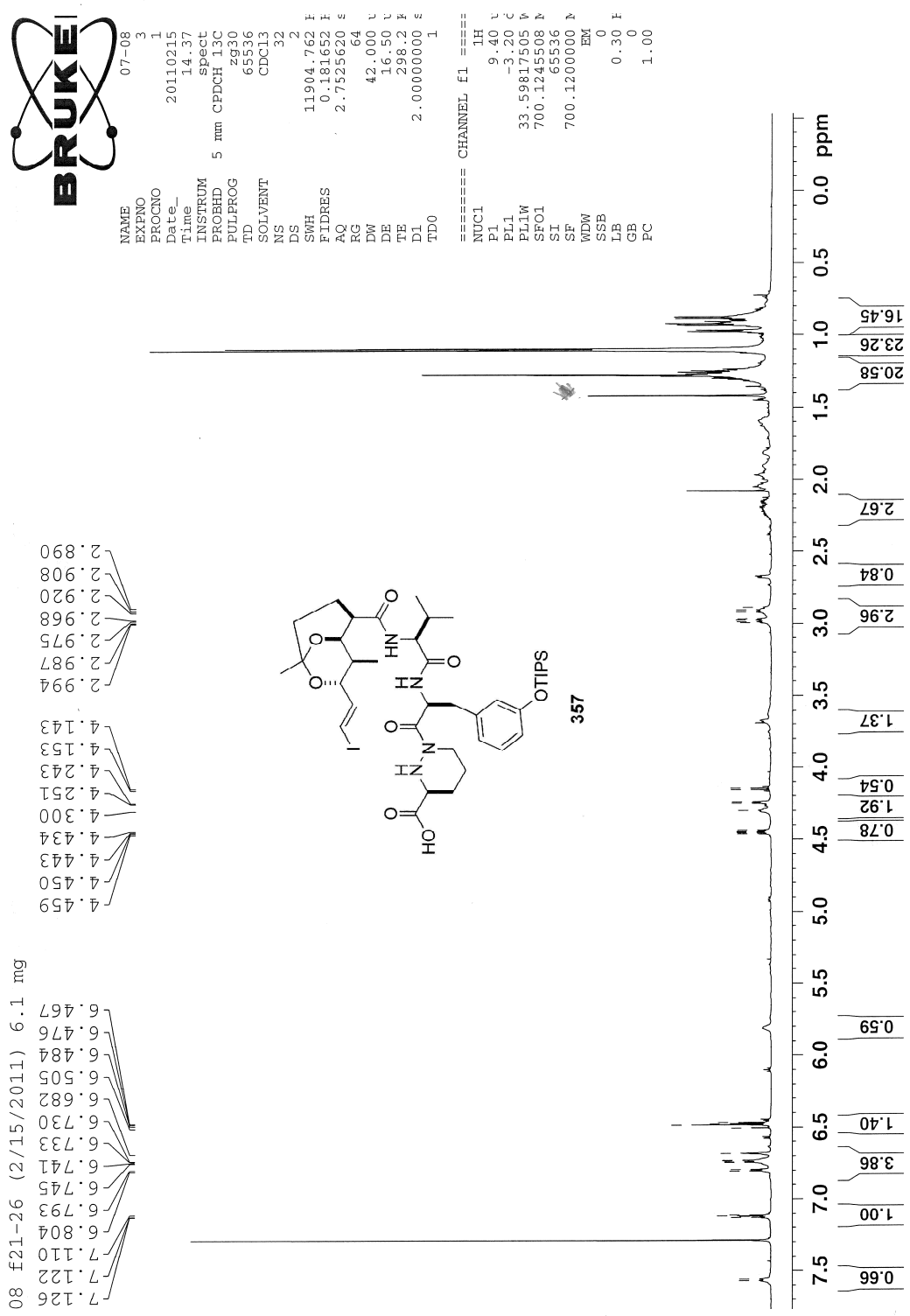

66 f3-4 (11/8/2010) 8.5 mg 13C
355
OTBS
I
NAME ks-T06-66-1
EXPNO 5
PROCNO 1
Date_ 20101108
Time 1.09
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 16331
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 14596.5
DW 20.850 u
DE 6.50 u
TE 300.2 K
D1 0.20000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
SFO1 100.6253446 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
SFO2 400.1416006 M
SI 32768
SF 100.6152830 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
149.98
149.93
83.04
77.64
77.30
77.19
76.98
76.66
43.18
30.33
29.68
25.75
24.89
24.83
24.73
24.70
19.58
18.21
-4.91
-5.08
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

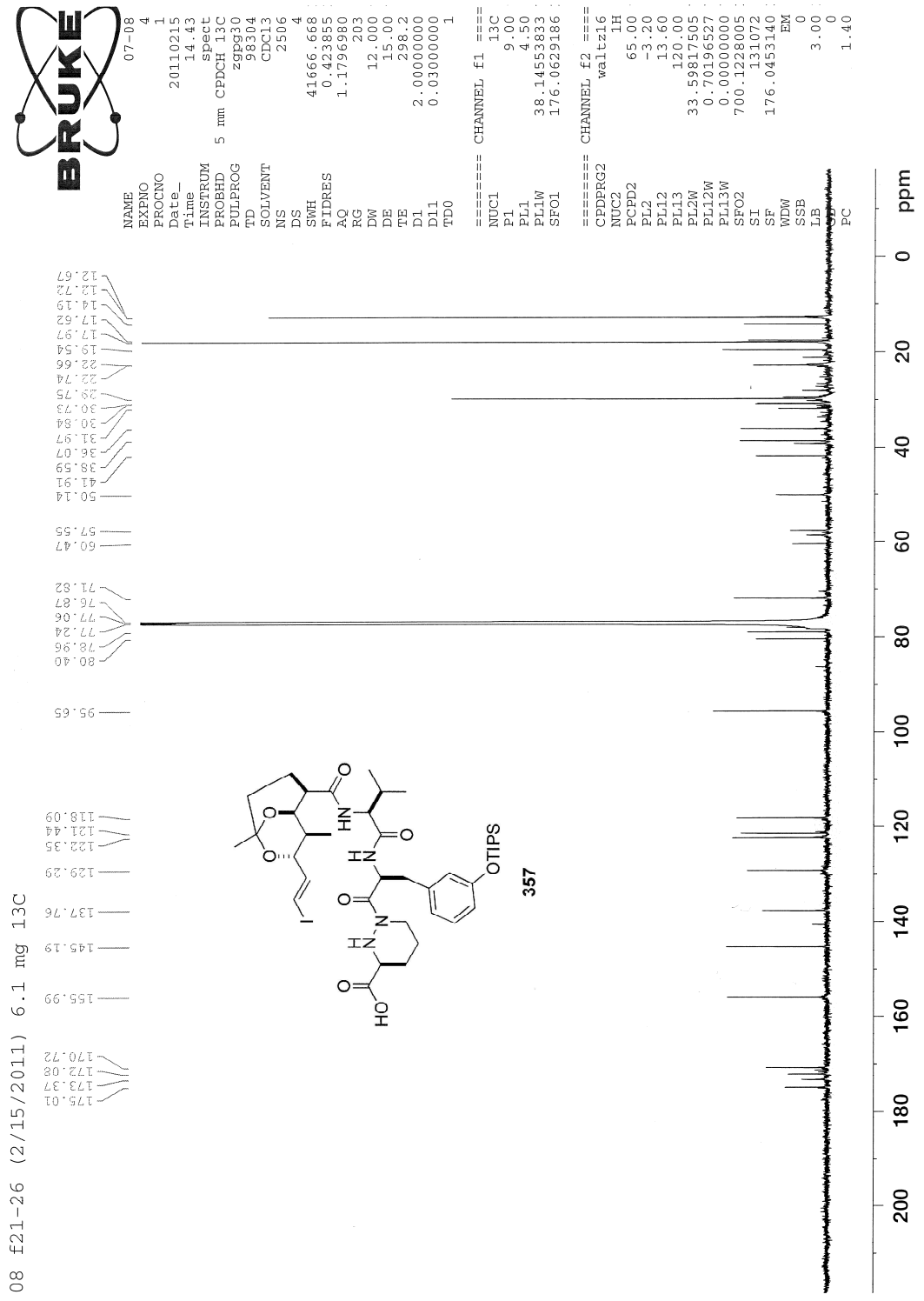

68 f5-15 (11/15/2010) 2.4 mg
NAME 68
EXPNO 1
PROCNO 1
Date_ 20101115
Time 1.20
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 32
DS 2
SWH 11904.762
FIDRES 0.181652
AQ 2.7525620
RG 64
DW 42.000
DE 16.50
TE 297.6
D1 2.00000000
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 9.40
PL1 -3.20
PL1W 33.59817505
SFO1 700.1245508
SI 65536
SF 700.1200000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
240
7.290
7.007
6.595
6.585
6.576
6.570
6.560
6.550
6.358
5.605
5.580
4.302
2.513
2.506
2.492
2.485
2.478
2.477
2.438
2.427
2.417
2.407
2.395
2.380
1.858
1.587
1.461
1.296
16.41
3.28
2.11
1.00
0.98
1.01
0.98
ppm

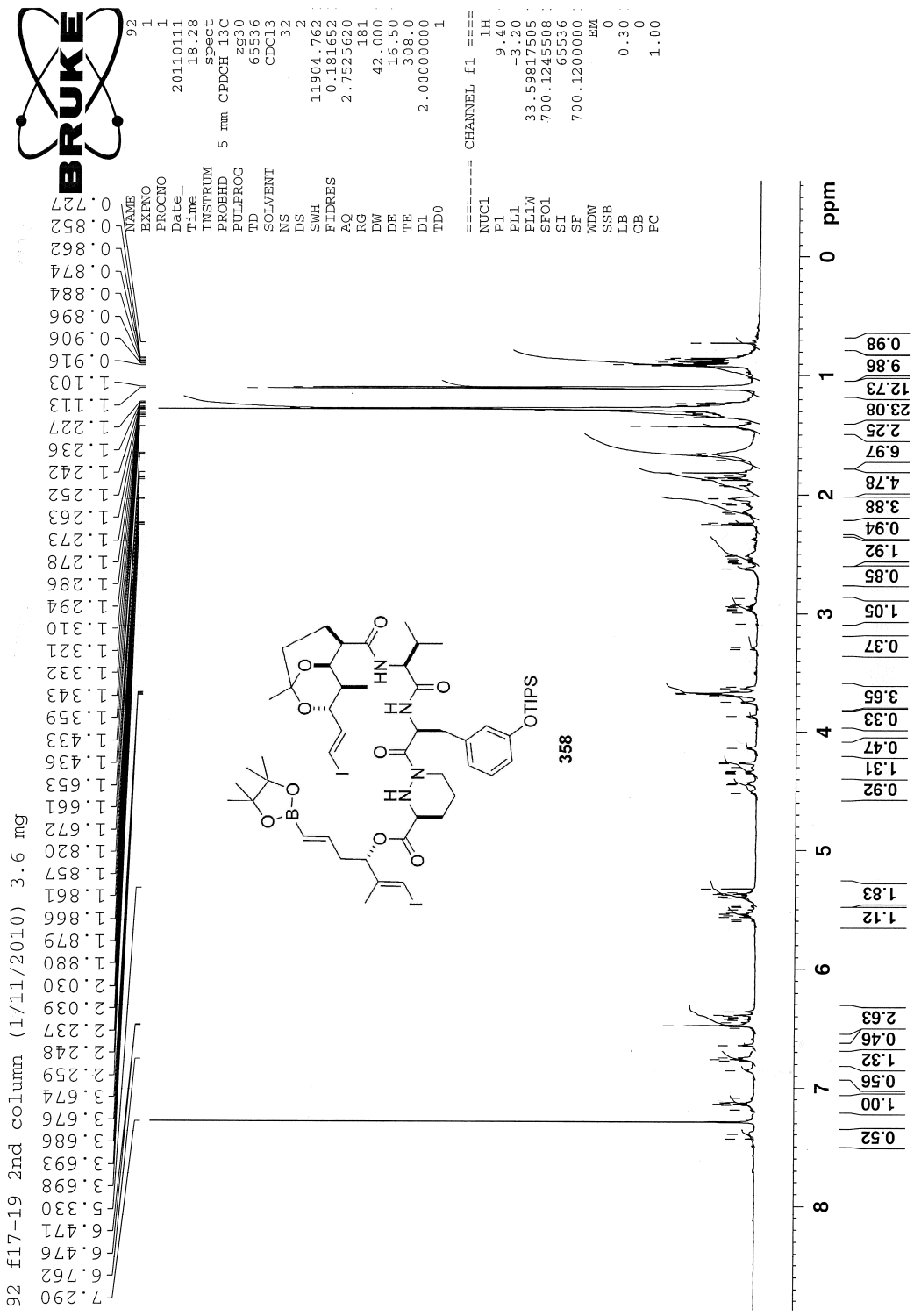

68 f5-15 (11/15/2010) 2.4 mg 13C
BRUKER
NAME 68
EXPNO 2
PROCNO 1
Date_ 20101115
Time 1.26
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 2720
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 297.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
83.31
78.75
77.21
77.03
76.85
75.12
42.03
30.34
29.72
24.80
24.78
20.19
149.04
148.70
240
200
180
160
140
120
100
80
60
40
20
0
ppm

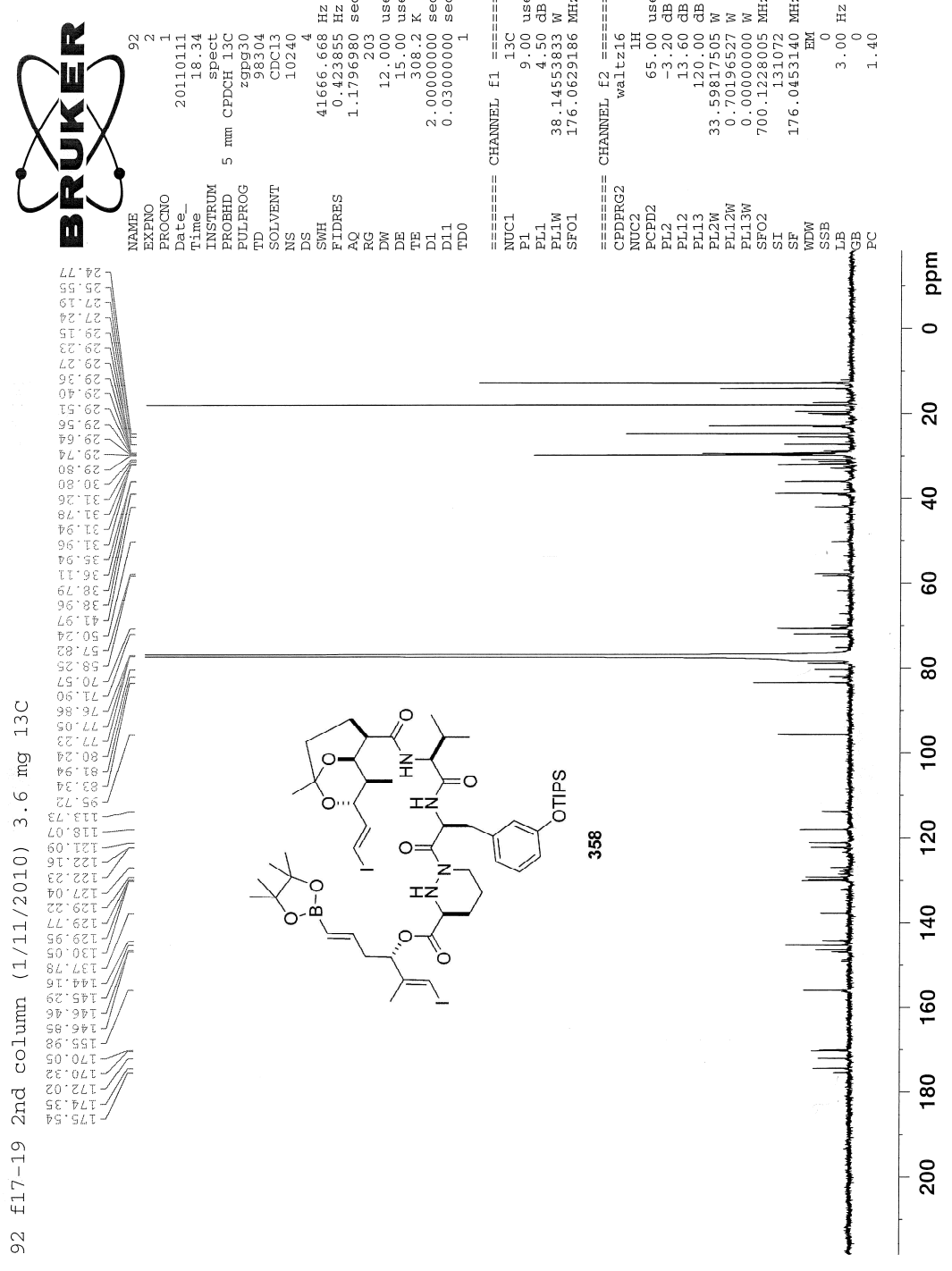

74 f7 (12/8/2010) 6.4 mg
NAME 74
EXPNO 1
PROCNO 1
Date_ 20101208
Time 16.35
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 32
DS 2
SWH 11904.762 H
FIDRES 0.181652 H
AQ 2.7525620 s
RG 64
DW 42.000 u
DE 16.50 u
TE 298.0 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 9.40 u
PL1 -3.20 d
PL1W 33.59817505 W
SFO1 700.1245508 M
SI 65536
SF 700.1200000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
MeO
OTIPS
356
ppm

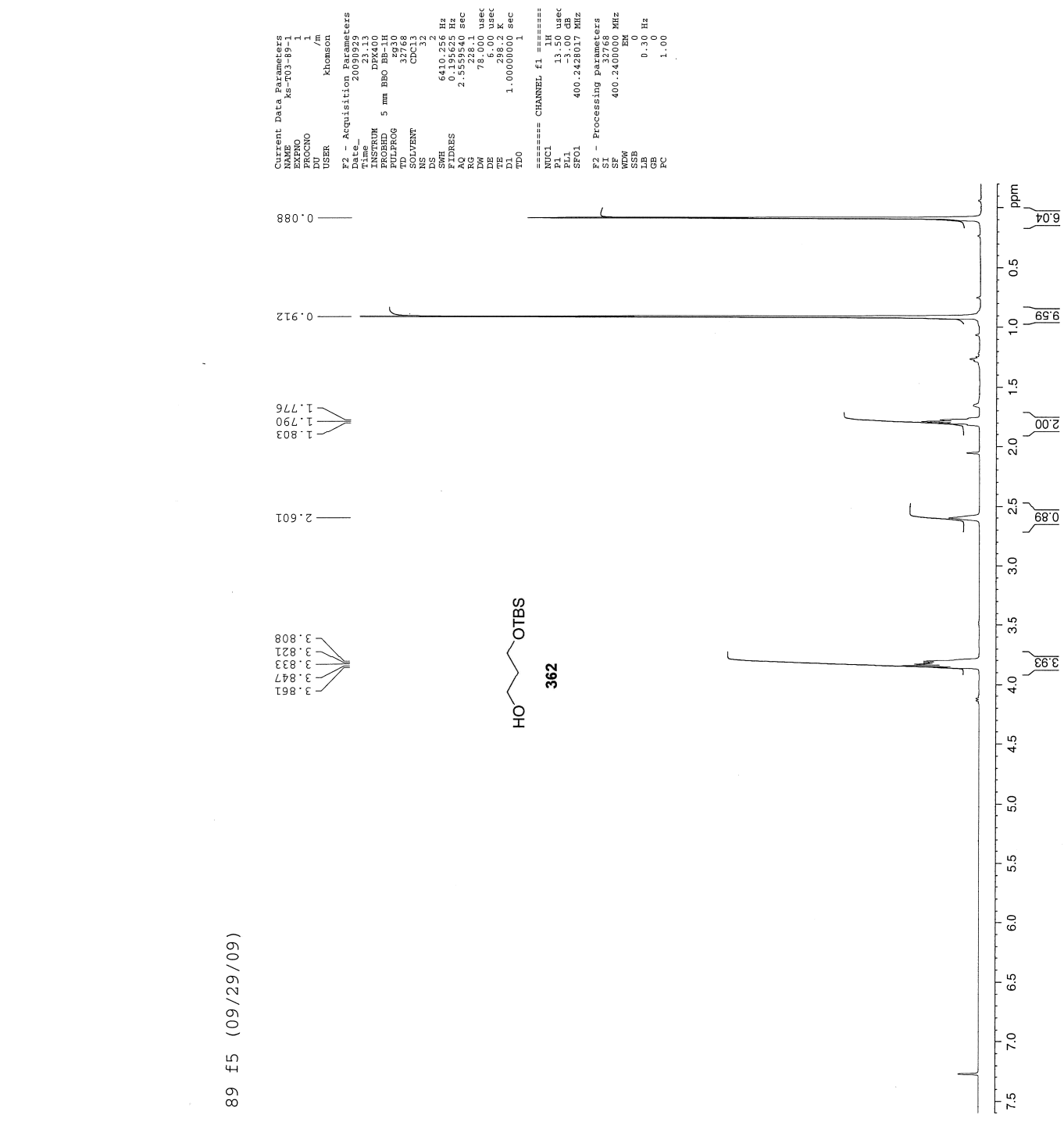

74 f7 (12/8/2010) 6.4 mg 13C
NAME 74
EXPNO 3
PROCNO 1
Date_ 20101208
Time 17.01
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 262
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
MeO
HN
NH
NH
N
O
OTIPS
I
356
ppm

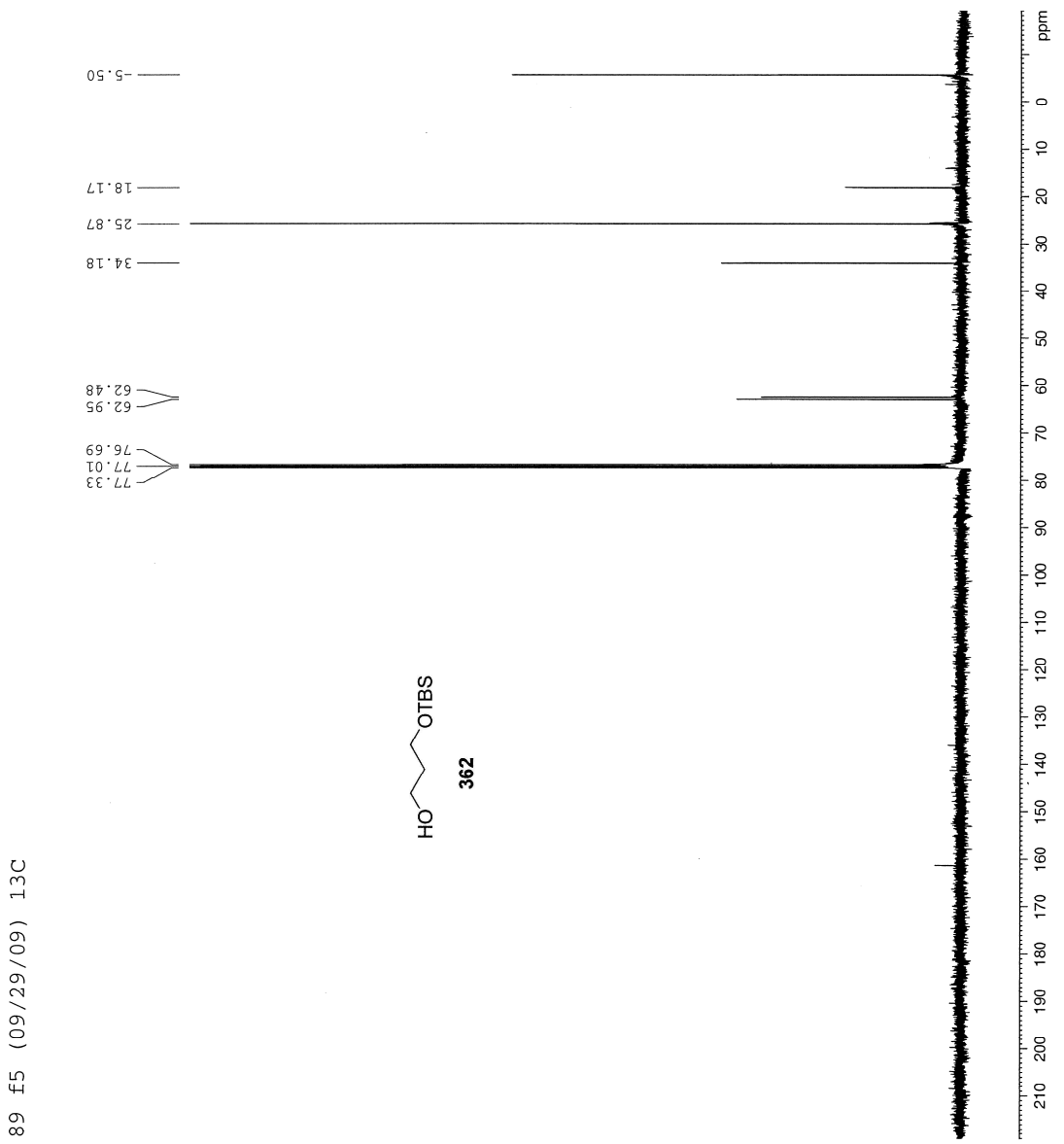

BRUKER
NAME 07-08
EXPNO 3
PROCNO 1
Date_ 20110215
Time 14.37
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 H
FIDRES 0.181652 H
AQ 2.7525620 s
RG 64
DW 42.000 u
DE 16.50 u
TE 298.2 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 1H
P1 9.40 u
PL1 -3.20 c
PL1W 33.59817505 W
SFO1 700.1245508 M
SI 65536
SF 700.1200000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
08 f21-26 (2/15/2011) 6.1 mg
7.126
7.122
7.110
6.804
6.793
6.745
6.741
6.733
6.730
6.682
6.505
6.484
6.476
6.467
4.459
4.450
4.443
4.434
4.300
4.251
4.243
4.153
4.143
2.994
2.987
2.975
2.968
2.920
2.908
2.890
HN
O
N
H
OTIPS
HO
I
357
ppm
0.66
1.00
3.86
1.40
0.59
0.78
1.92
0.54
1.37
2.96
0.84
2.67
20.58
23.26
16.45

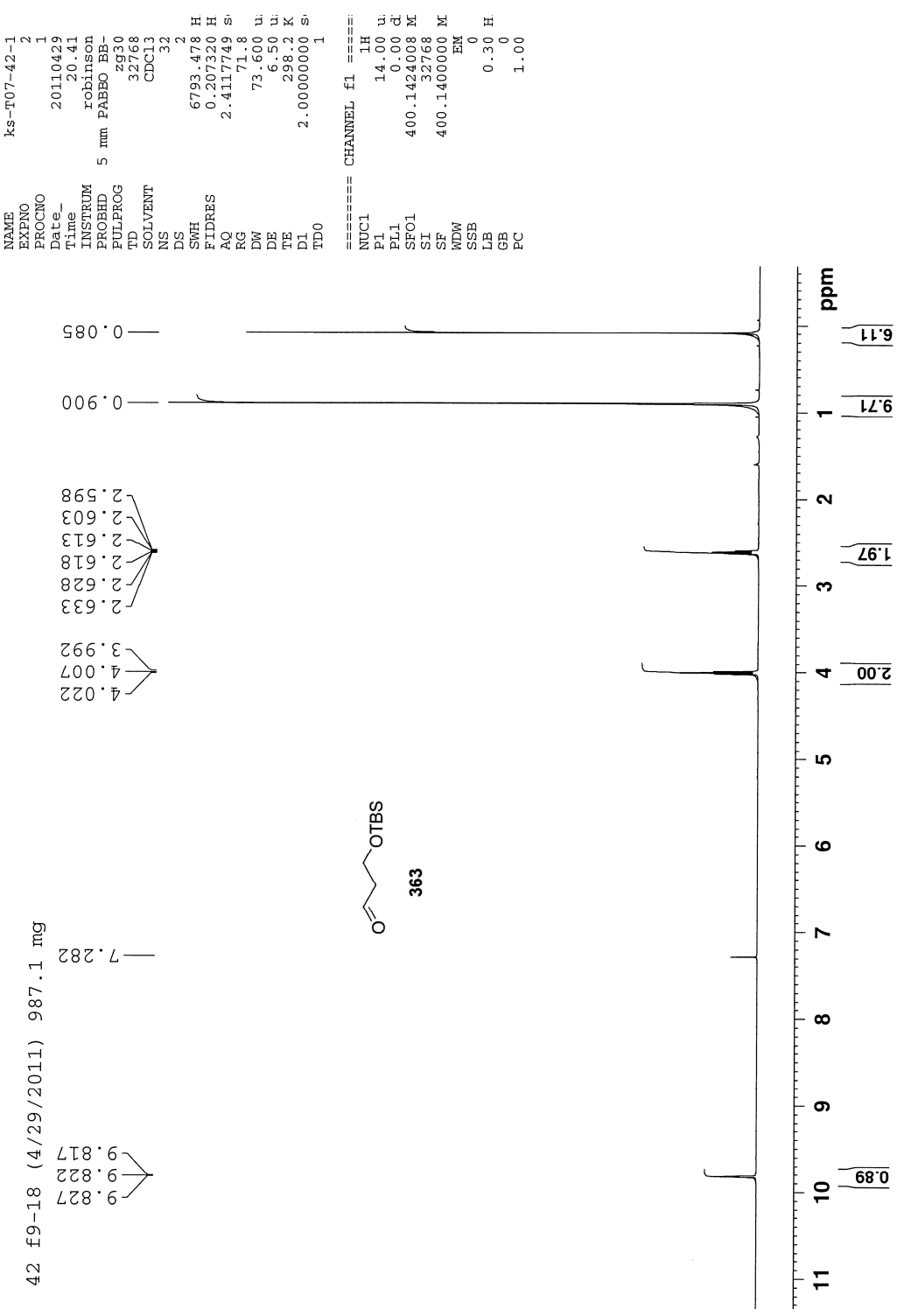

08 f21-26 (2/15/2011) 6.1 mg 13C
NAME 07-08
EXPNO 4
PROCNO 1
Date_ 20110215
Time 14.43
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 2506
DS 4
SWH 41666.668
FIDRES 0.423855
AQ 1.1796980
RG 203
DW 12.000
DE 15.00
TE 298.2
D1 2.00000000
D11 0.03000000
TDO 1
NUC1 13C
P1 9.00
PL1 4.50
PL1W 38.14553833
SFO1 176.0629186
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00
PL2 -3.20
PL12 13.60
PL13 120.00
PL2W 33.59817505
PL12W 0.70196527
PL13W 0.00000000
SFO2 700.1228005
SI 131072
SF 176.0453140
WDW EM
SSB 0
LB 3.00
GB 0
PC 1.40
175.01
173.37
172.08
170.72
145.19
137.76
129.29
122.35
121.44
118.09
95.65
80.40
78.96
77.24
76.87
71.82
60.47
57.55
50.14
41.91
38.59
36.07
34.97
30.84
30.73
29.75
22.74
22.66
19.54
17.97
17.62
14.19
12.72
12.67
200
180
160
140
120
100
80
60
40
20
0
ppm
357

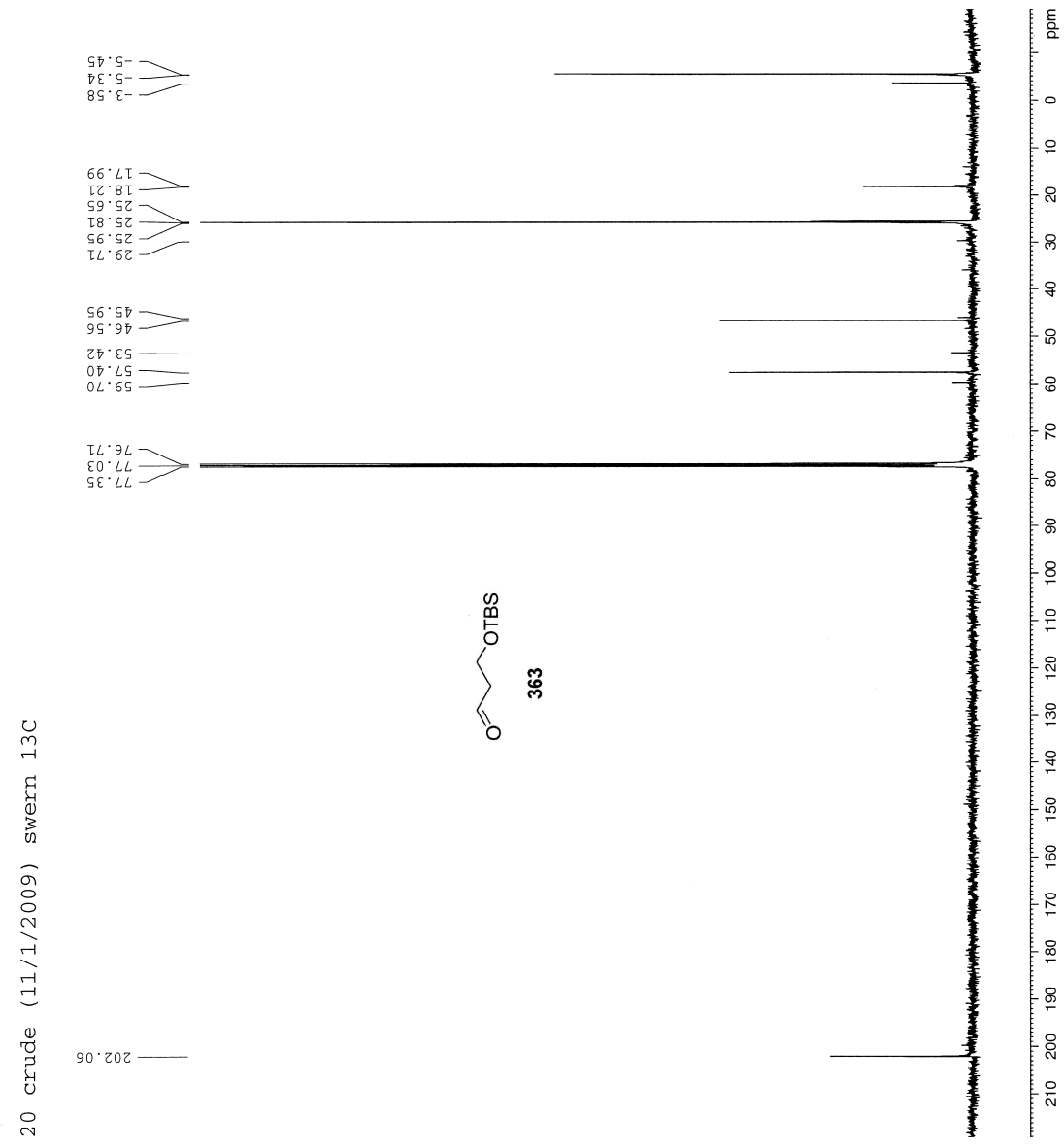

92 f17-19 2nd column (1/11/2010) 3.6 mg
BRUKER
358
OTIPS
ppm

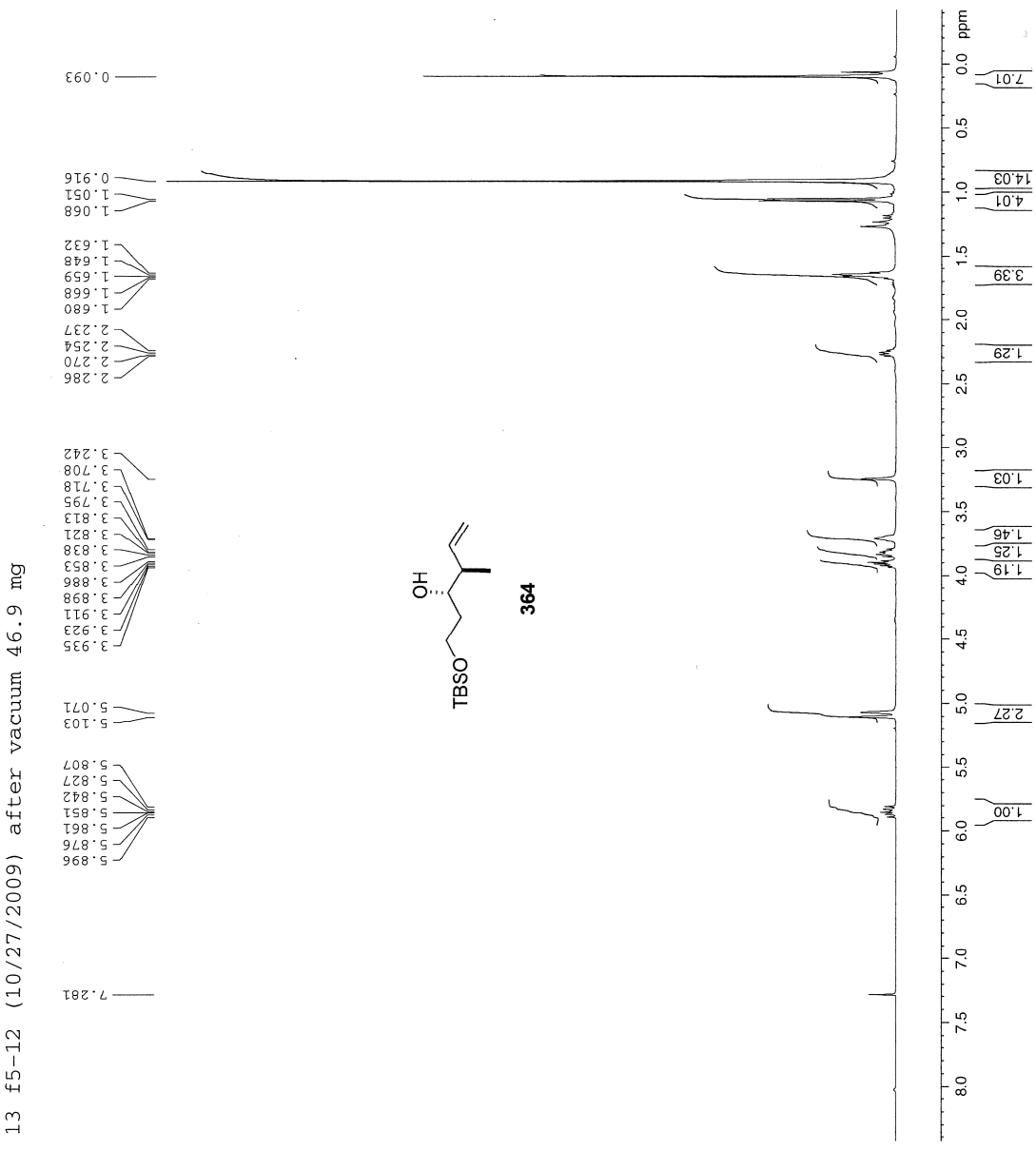

92 f17-19 2nd column (1/11/2010) 3.6 mg 13C
BRUKER
NAME 92
EXPNO 2
PROCNO 1
Date_ 20110111
Time 18.34
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 10240
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 308.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OTIPS
358
200 180 160 140 120 100 80 60 40 20 0 ppm

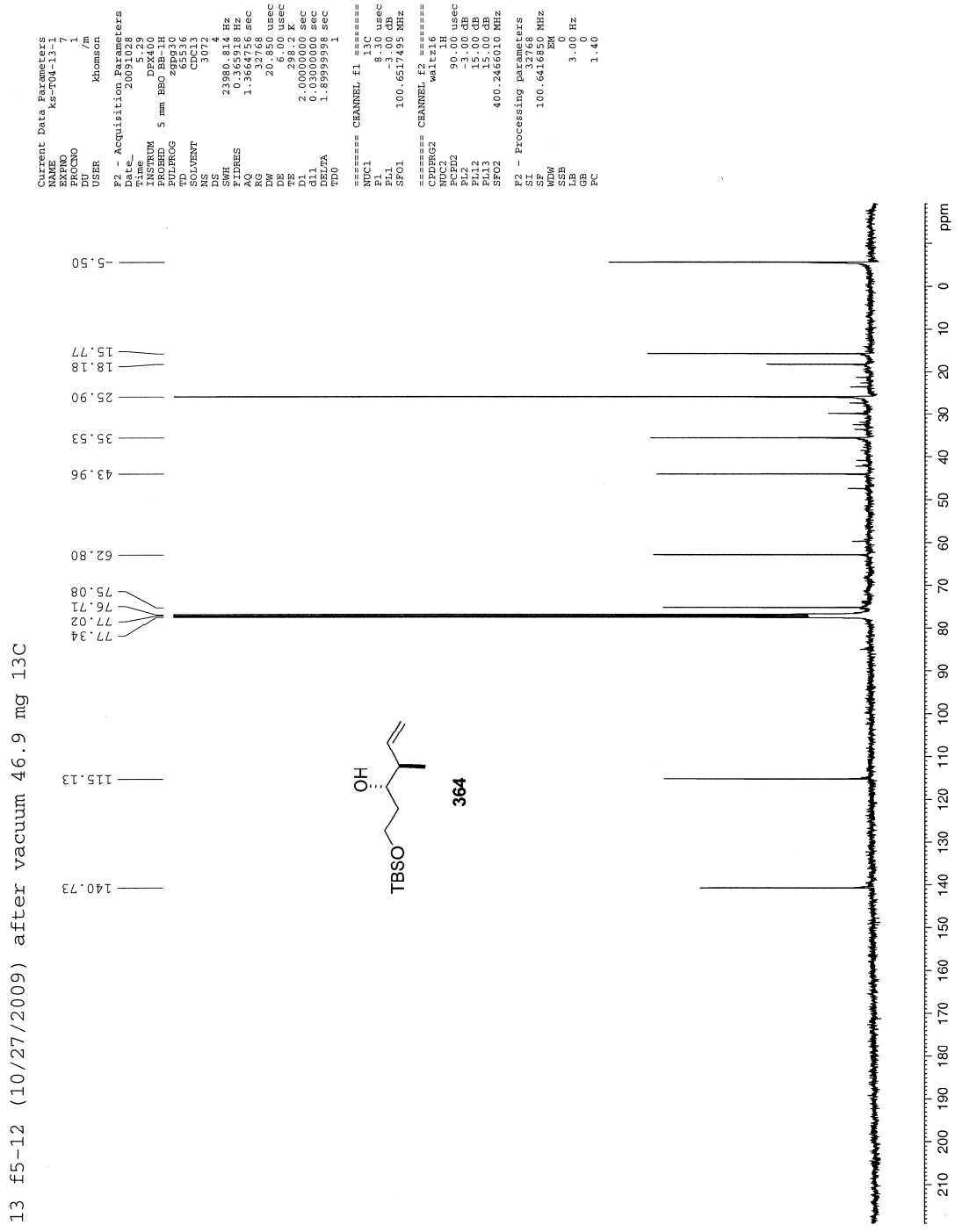

Current Data Parameters
NAME Ks-TO3-89-1
EXPNO 1
PROCNO 1
DU /m
USER khomson
P2 - Acquisition Parameters
Date_ 20090929
Time 21.33
INSTRUM DRX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 228.1
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2428017 MHz
P2 - Processing parameters
SI 32768
SF 400.2400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
0.088
0.912
1.776
1.790
1.803
2.601
3.808
3.821
3.833
3.847
3.861
HO
OTBS
362
6.04
9.59
2.00
0.89
3.93
ppm
89 f5 (09/29/09)

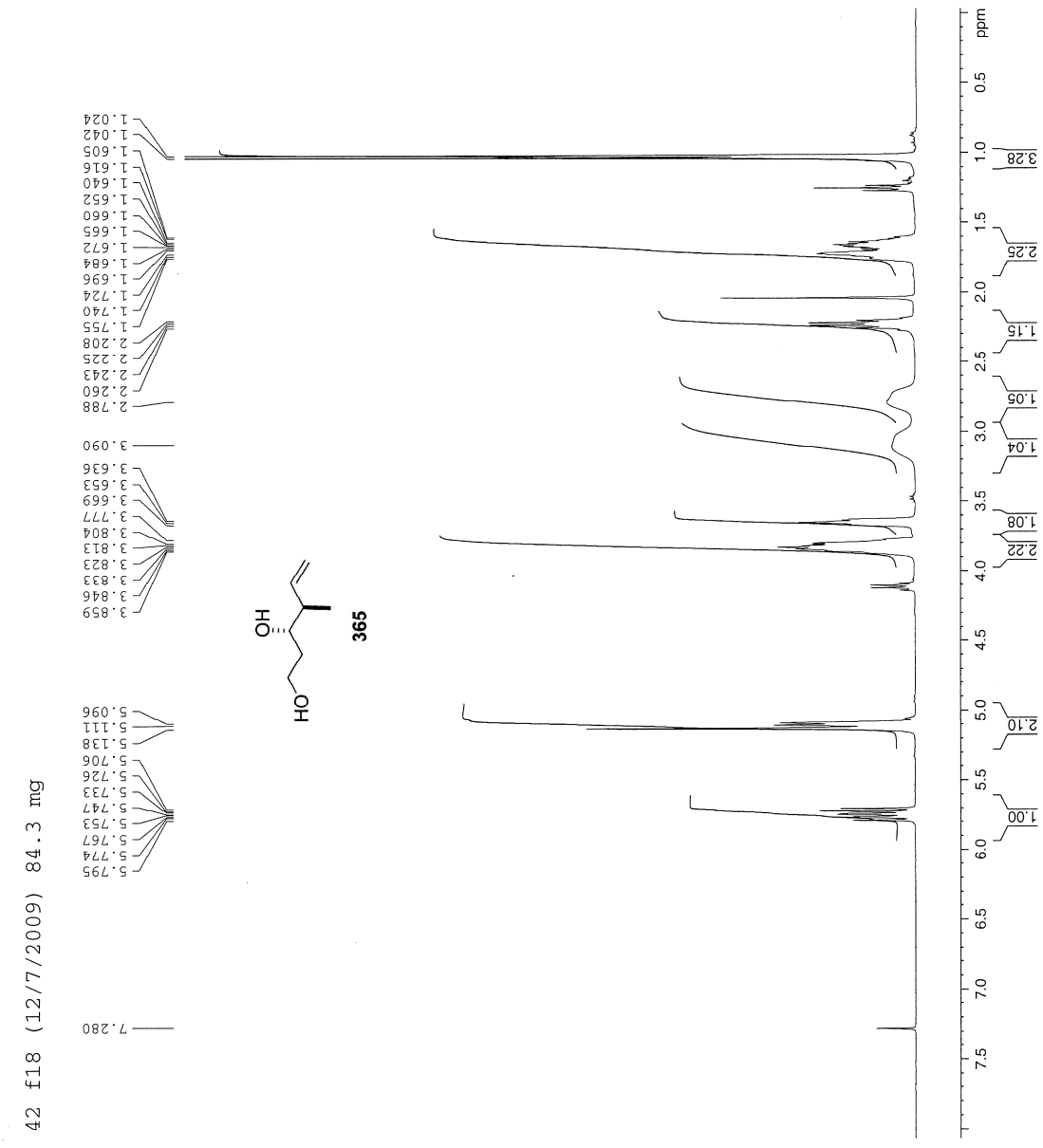

89 f5 (09/29/09) 13C
Current Data Parameters
NAME ks-TV3-89-1
EXPNO 5
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20090930
Time 1.05
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 2048
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6504921 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.1416010 MHz
F2 - Processing parameters
SI 32768
SF 100.6402863 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
-5.50
18.17
25.87
34.18
62.48
62.95
76.69
77.01
77.33
HO
OTBS
362
ppm

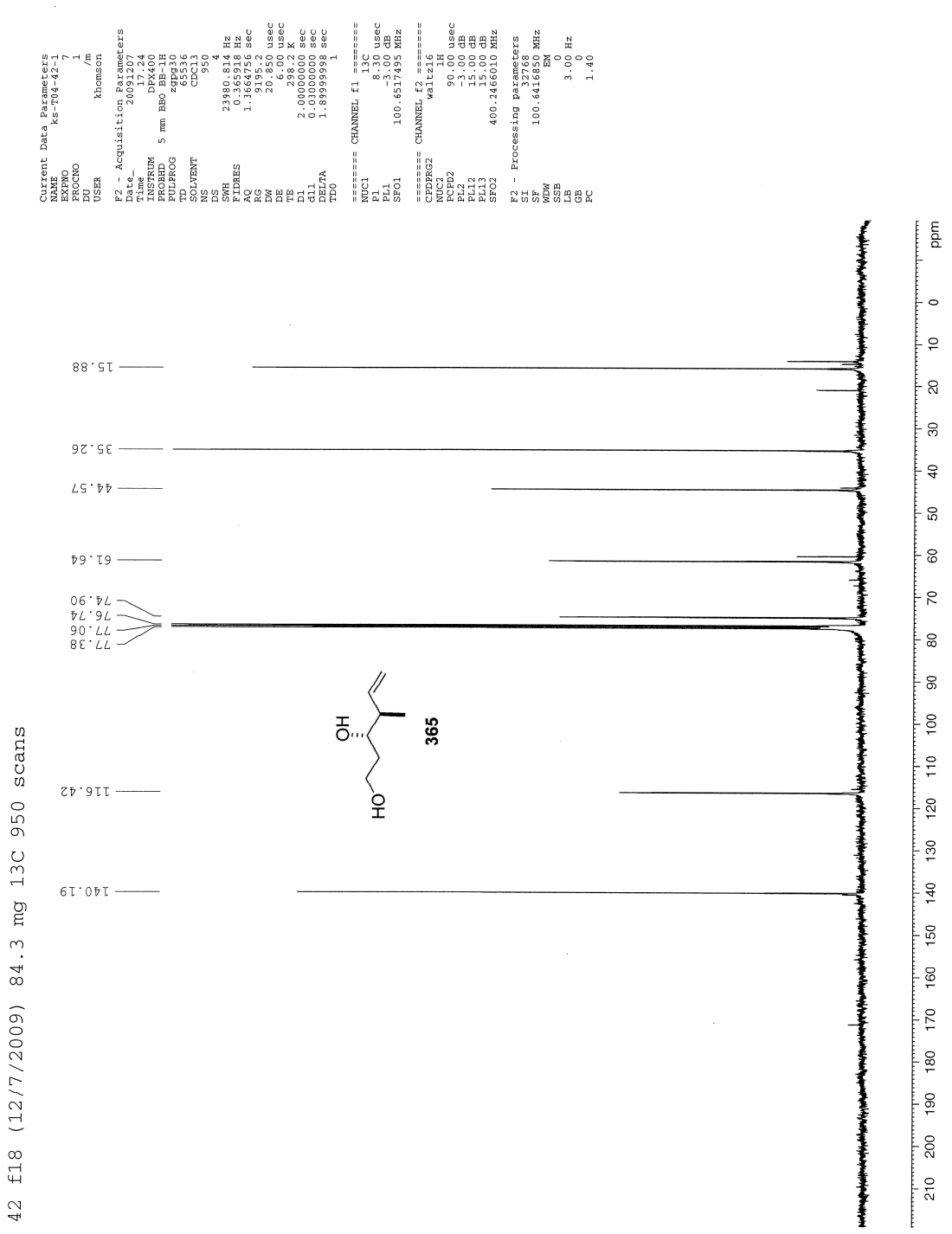

NAME ks-T07-42-1
EXPNO 2
PROCNO 1
Date_ 20110429
Time 20.41
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 71.8
DW 73.600 u
DE 6.50 u
TE 298.2 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
42 f9-18 (4/29/2011) 987.1 mg
OTBS
363
9.827
9.822
9.817
7.282
4.022
4.007
3.992
2.633
2.628
2.618
2.613
2.603
2.598
0.900
0.085
ppm
0.89
2.00
1.97
9.71
6.11

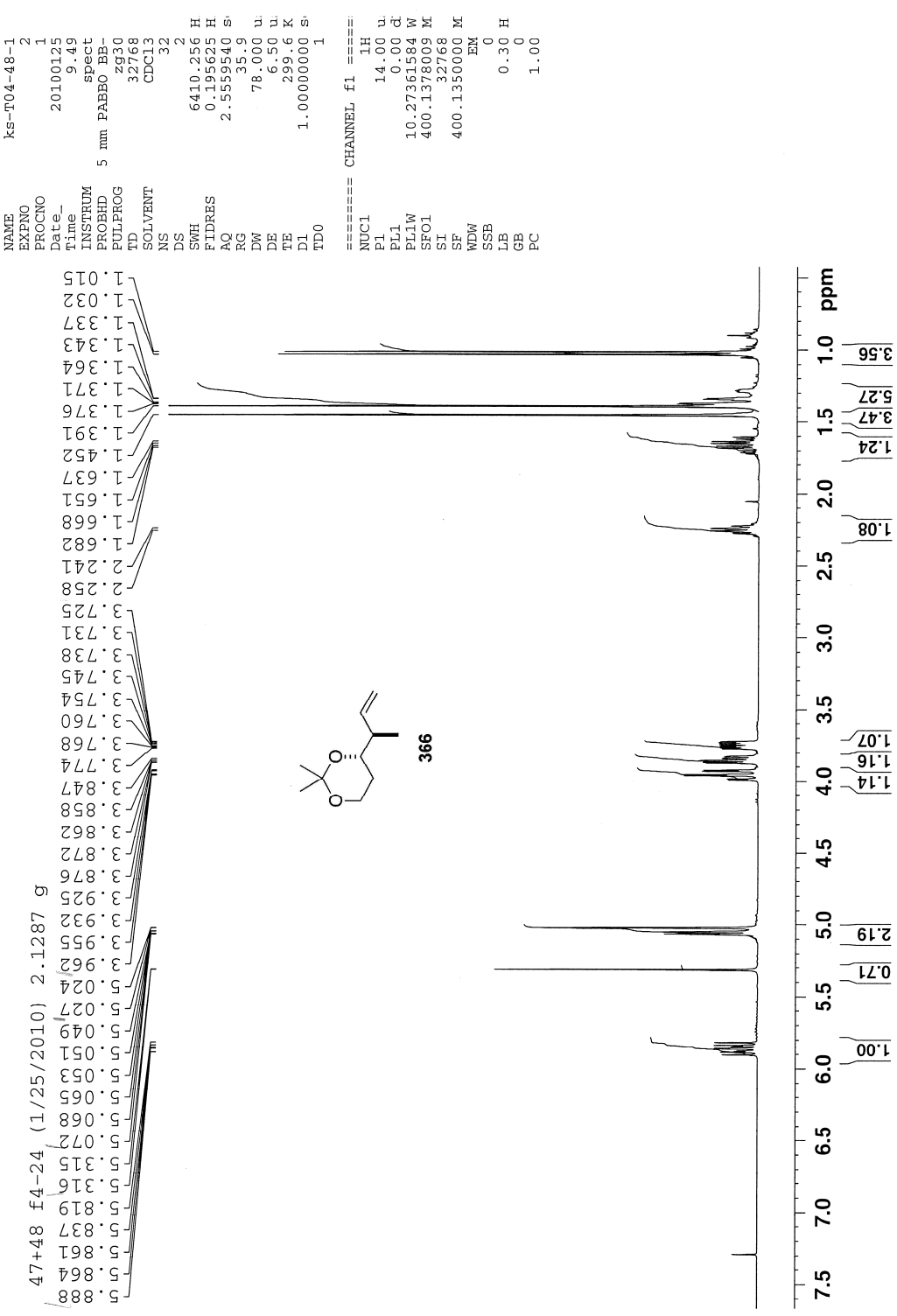

20 crude (11/1/2009) swern 13C
Current Data Parameters
NAME ks-T04-20-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091101
Time 15.37
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
202.06
77.35
77.03
76.71
59.70
57.40
53.42
46.56
45.95
29.71
25.95
25.81
25.65
18.21
17.99
-5.34
-5.45
OTBS
O
363
ppm

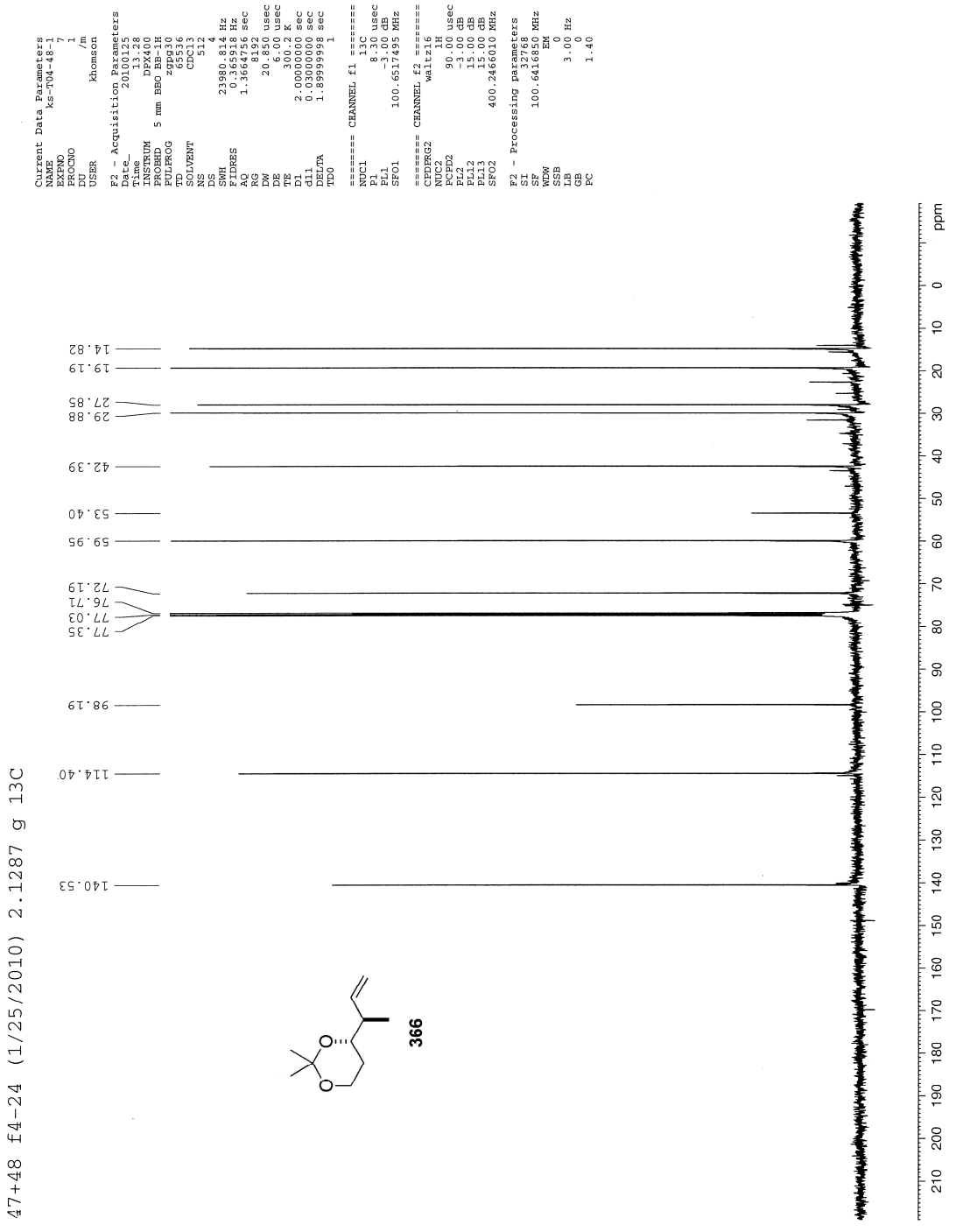

13 f5-12 (10/27/2009) after vacuum 46.9 mg
Current Data Parameters
NAME ks-T04-13-1
EXPNO 3
PROCNO 1
DU /m
USER khomson
P2 - Acquisition Parameters
Date_ 20091027
Time_ 22.58
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55599540 sec
RG 143.7
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
P2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
TBSO
364
0.093
0.916
1.051
1.068
1.632
1.648
1.659
1.668
1.680
2.237
2.254
2.270
2.286
3.242
3.708
3.718
3.795
3.813
3.821
3.838
3.853
3.886
3.898
3.911
3.923
3.935
5.071
5.103
5.807
5.827
5.842
5.851
5.861
5.876
5.896
7.281
ppm
7.01
14.03
4.01
3.39
1.29
1.03
1.46
1.25
1.19
2.27
1.00

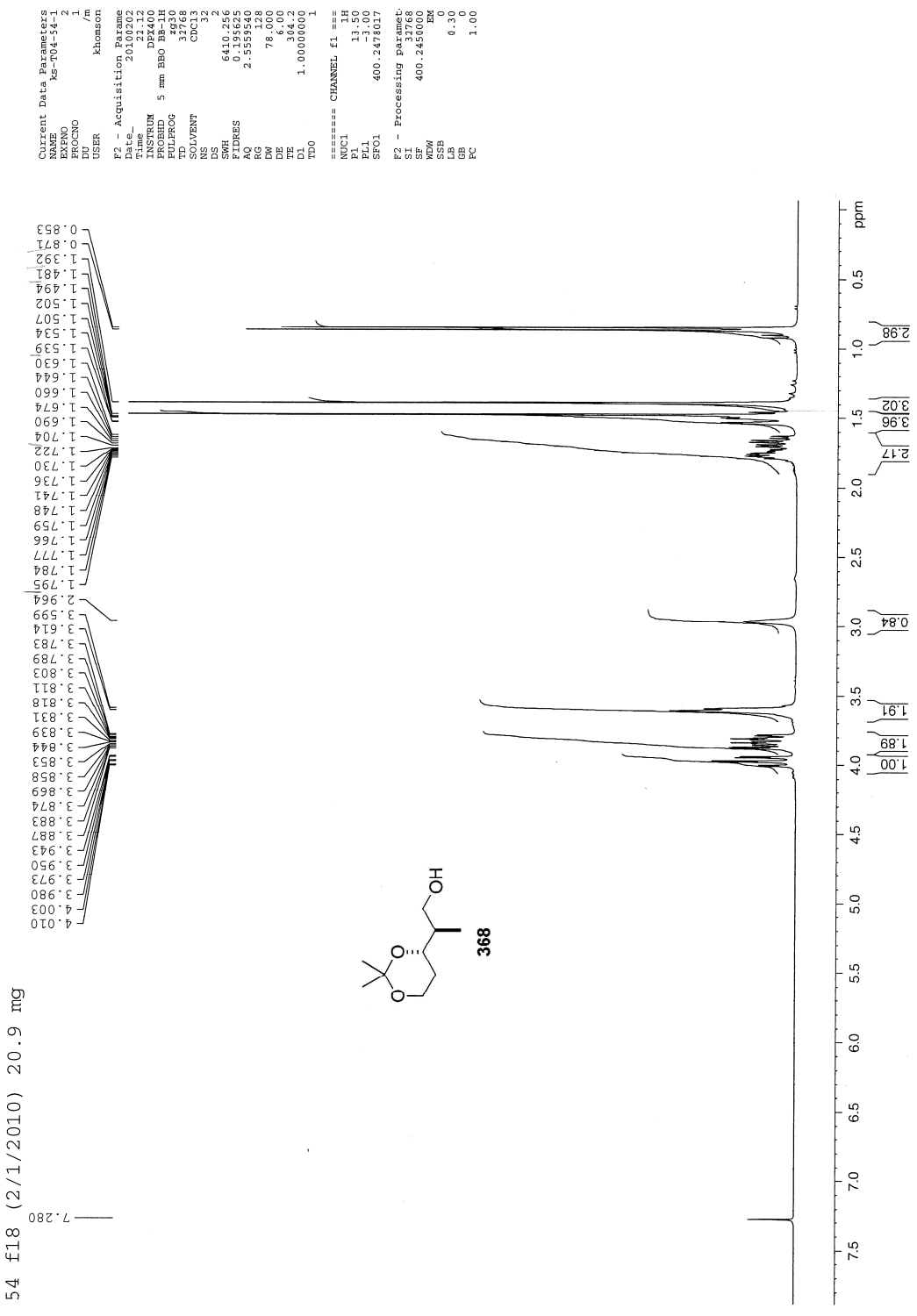

13 f5-12 (10/27/2009) after vacuum 46.9 mg 13C
Current Data Parameters
NAME ks-T04-13-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091028
Time 5.29
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3072
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.36644756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
-5.50
15.77
18.18
25.90
35.53
43.96
62.80
75.08
76.71
77.02
77.34
115.13
140.73
OH
TBSO
364
ppm

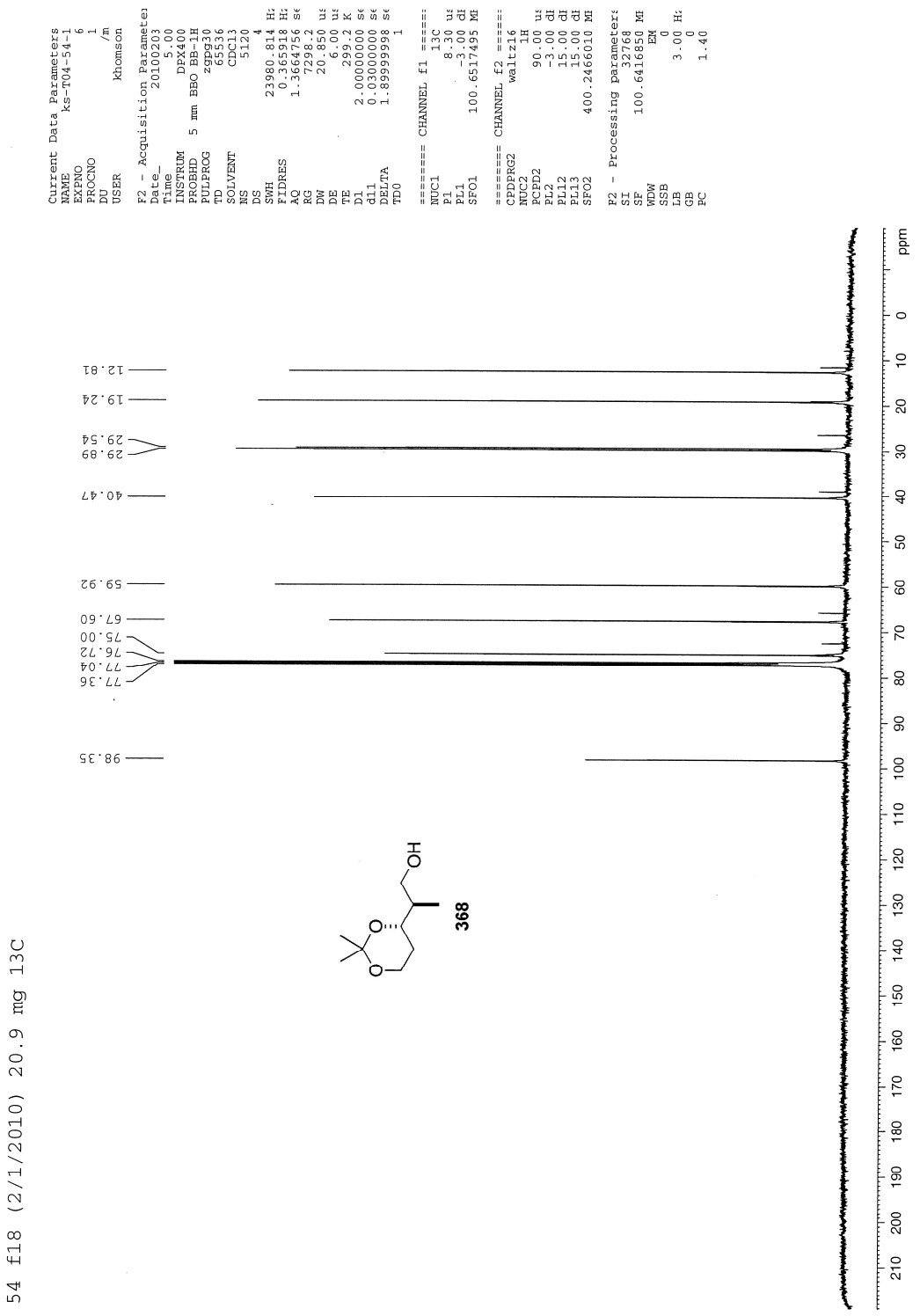

42 f18 (12/7/2009) 84.3 mg
Current Data Parameters
NAME ks-f04-42-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091207
Time 13.21
INSTRUM DPX400
PROBHD 5 mm BBO BA-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5557540 sec
RG 71.58
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.280
5.795
5.774
5.767
5.753
5.747
5.733
5.726
5.706
5.138
5.111
5.096
3.859
3.846
3.833
3.823
3.813
3.804
3.777
3.669
3.653
3.636
3.090
2.788
2.260
2.243
2.225
2.208
1.755
1.740
1.724
1.696
1.684
1.672
1.665
1.660
1.652
1.640
1.616
1.605
1.042
1.024
OH
HO
365
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.00
2.10
1.00
2.22
1.08
1.04
1.05
1.15
2.25
3.28

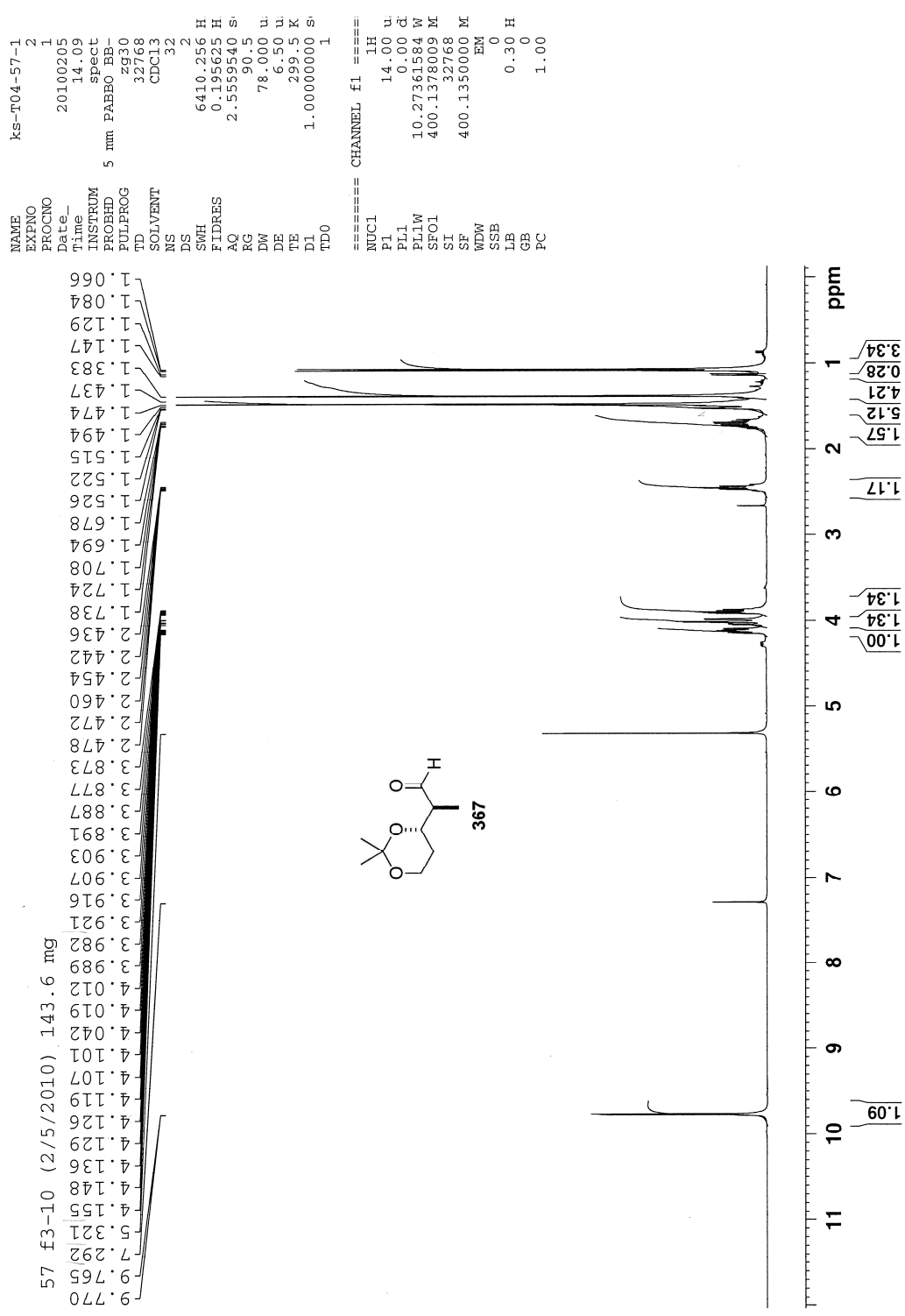

42 f18 (12/7/2009) 84.3 mg 13C 950 scans
Current Data Parameters
NAME ks-T04-42-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20091207
Time_ 17.24
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 950
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 9195.2
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 2.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
15.88
35.26
44.57
61.64
74.90
76.74
77.06
77.38
116.42
140.19
OH
HO
365
ppm

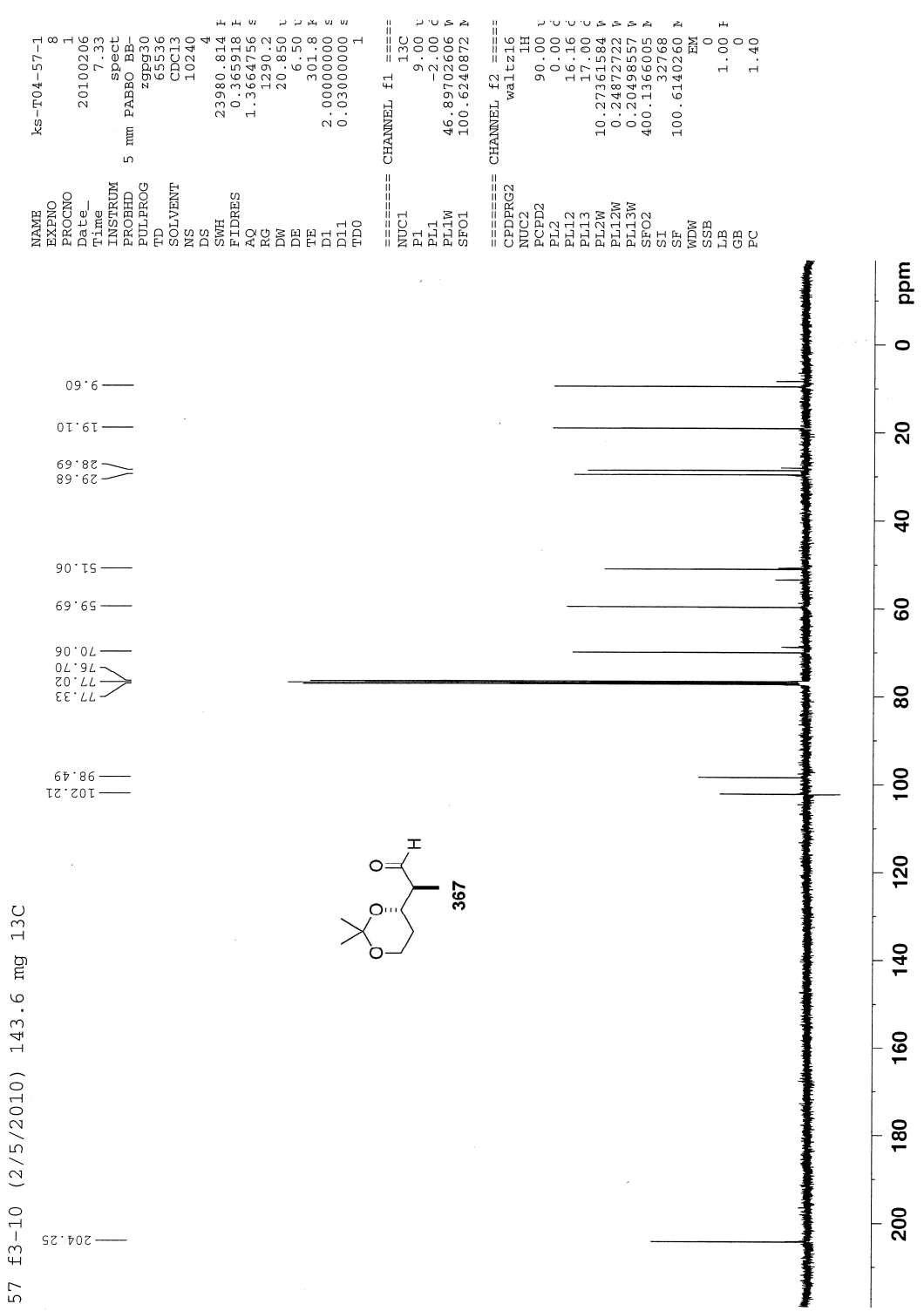

NAME ks-T04-48-1
EXPNO 2
PROCNO 1
Date_ 20100125
Time_ 9.49
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.55599540 s
RG 35.9
DW 78.000 u
DE 6.50 u
TE 299.6 K
D1 1.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1378009 M
SI 32768
SF 400.1350000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
47+48 f4-24 (1/25/2010) 2.1287 g
366
ppm
3.56
5.27
3.47
1.24
1.08
1.07
1.16
1.14
2.19
0.71
1.00

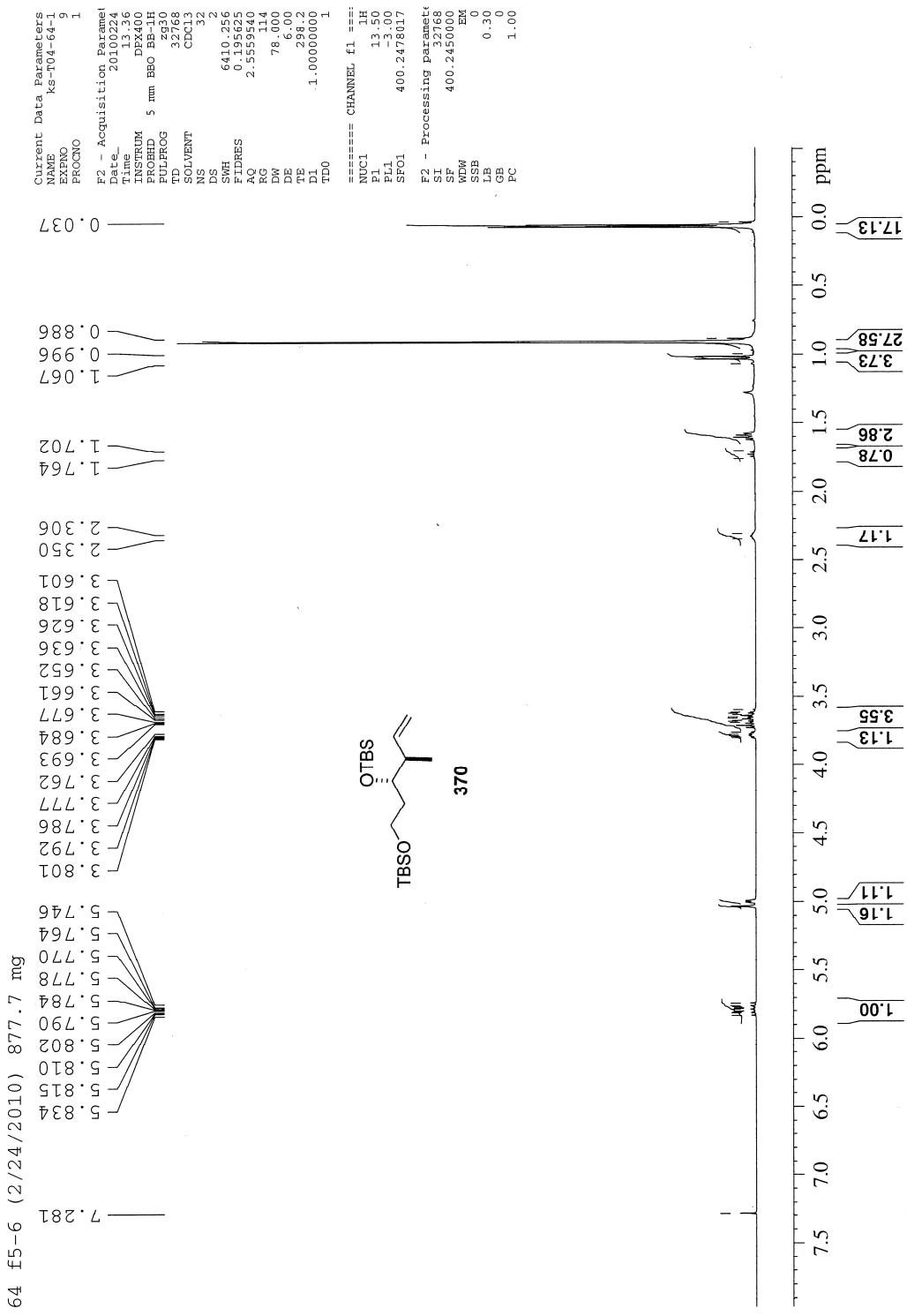

47+48 f4-24 (1/25/2010) 2.1287 g 13C
Current Data Parameters
NAME ks-T04-48-1
EXPNO 7
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20100125
Time 13.28
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 130
DW 20.850 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
14.82
19.19
27.85
29.88
42.39
53.40
59.95
72.19
76.71
77.03
77.35
98.19
114.40
140.53
366
ppm

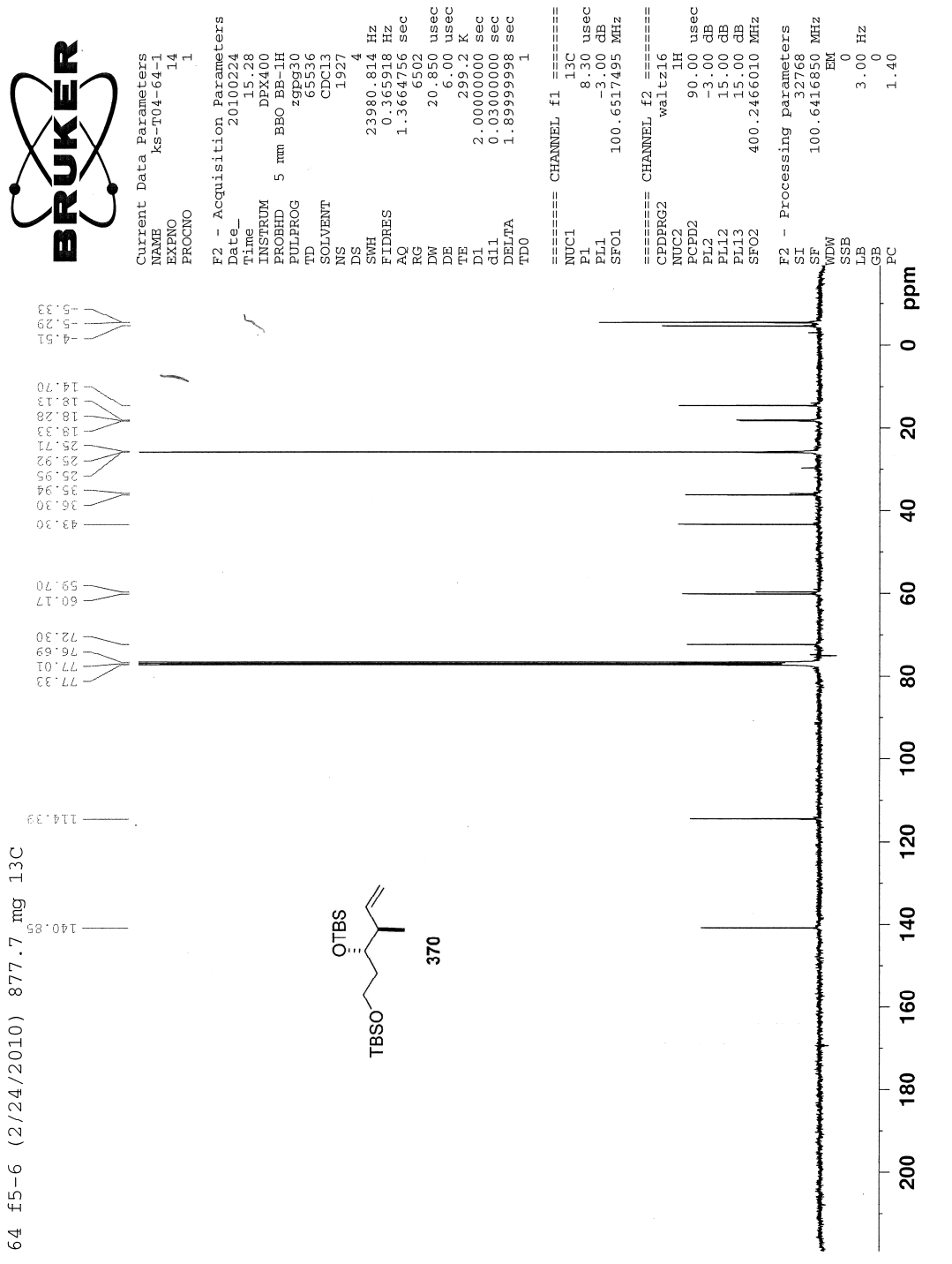

54 f18 (2/1/2010) 20.9 mg
368
OH
O
O
7.280
4.010
4.003
3.980
3.973
3.950
3.943
3.887
3.883
3.874
3.869
3.858
3.853
3.844
3.839
3.831
3.818
3.811
3.803
3.789
3.783
3.614
3.599
2.964
1.795
1.784
1.777
1.766
1.759
1.748
1.741
1.736
1.730
1.722
1.704
1.690
1.674
1.660
1.644
1.630
1.539
1.534
1.507
1.502
1.494
1.481
1.392
0.871
0.853
Current Data Parameters
NAME ks-T04-54-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parame
Date_ 20100202
Time 22.13
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 128
DW 78.000
DE 6.00
TE 304.2
D1 1.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 13.50
PL1 -3.00
SFO1 400.2478017
F2 - Processing paramet
SI 32768
SF 400.2450000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
2.98
3.02
3.96
2.17
0.84
1.91
1.89
1.00
ppm

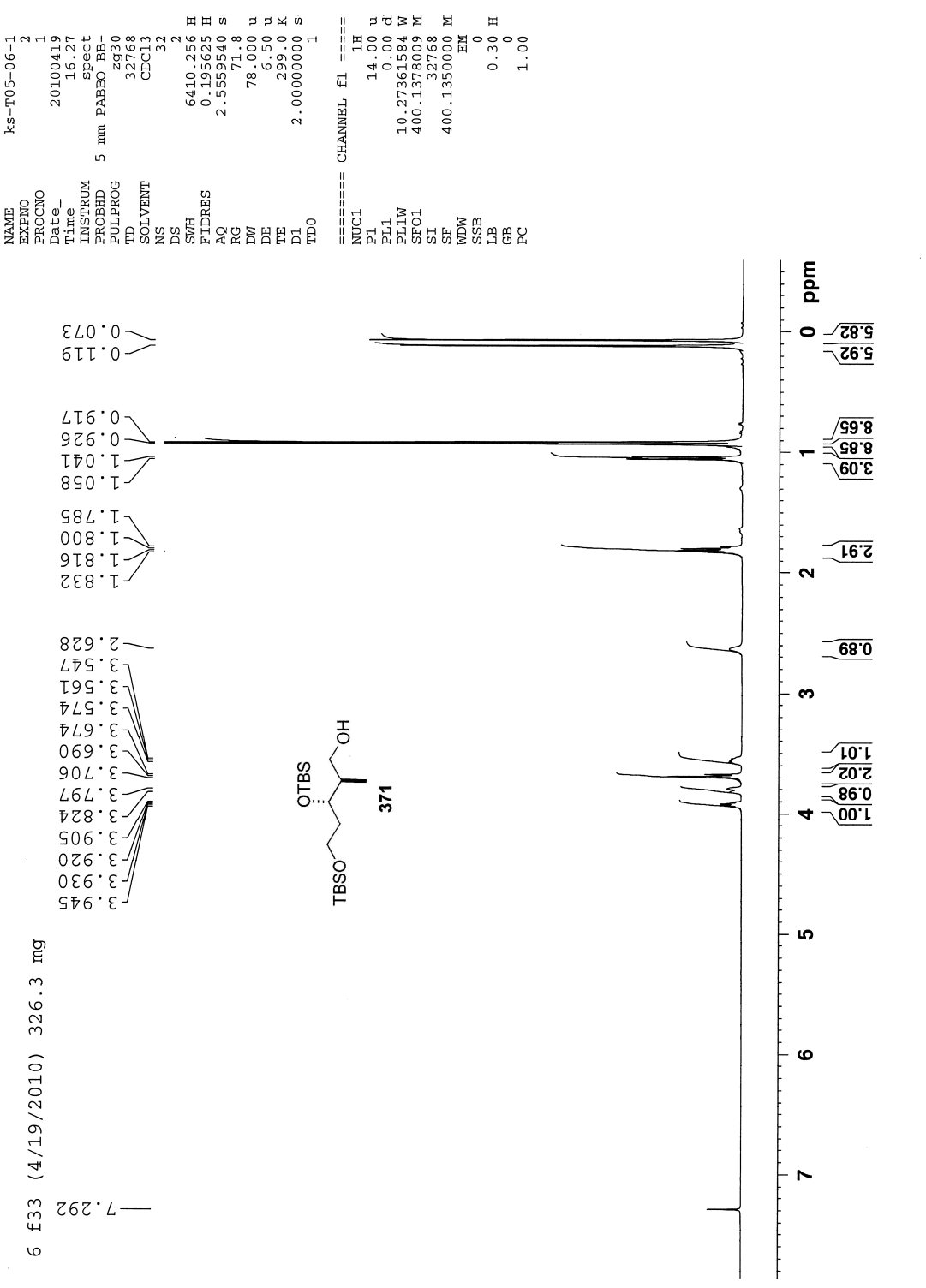

54 f18 (2/1/2010) 20.9 mg 13C
Current Data Parameters
NAME ks-T04-54-1
EXPNO 6
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameter
Date_ 20100203
Time_ 5.00
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 5120
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 7298.2
DW 20.850 u
DE 6.00 u
TE 299.2 K
D1 2.00000000 s
d11 0.03000000 s
DELTA 1.89999998 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 8.30 u
PL1 -3.00 d
SFO1 100.6517495 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 -3.00 d
PL12 15.00 d
PL13 15.00 d
SFO2 400.2466010 M
F2 - Processing parameter
SI 32768
SF 100.6416850 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
12.81
19.24
29.54
29.89
40.47
59.92
67.60
75.00
76.72
77.04
77.36
98.35
OH
O
O
368
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210

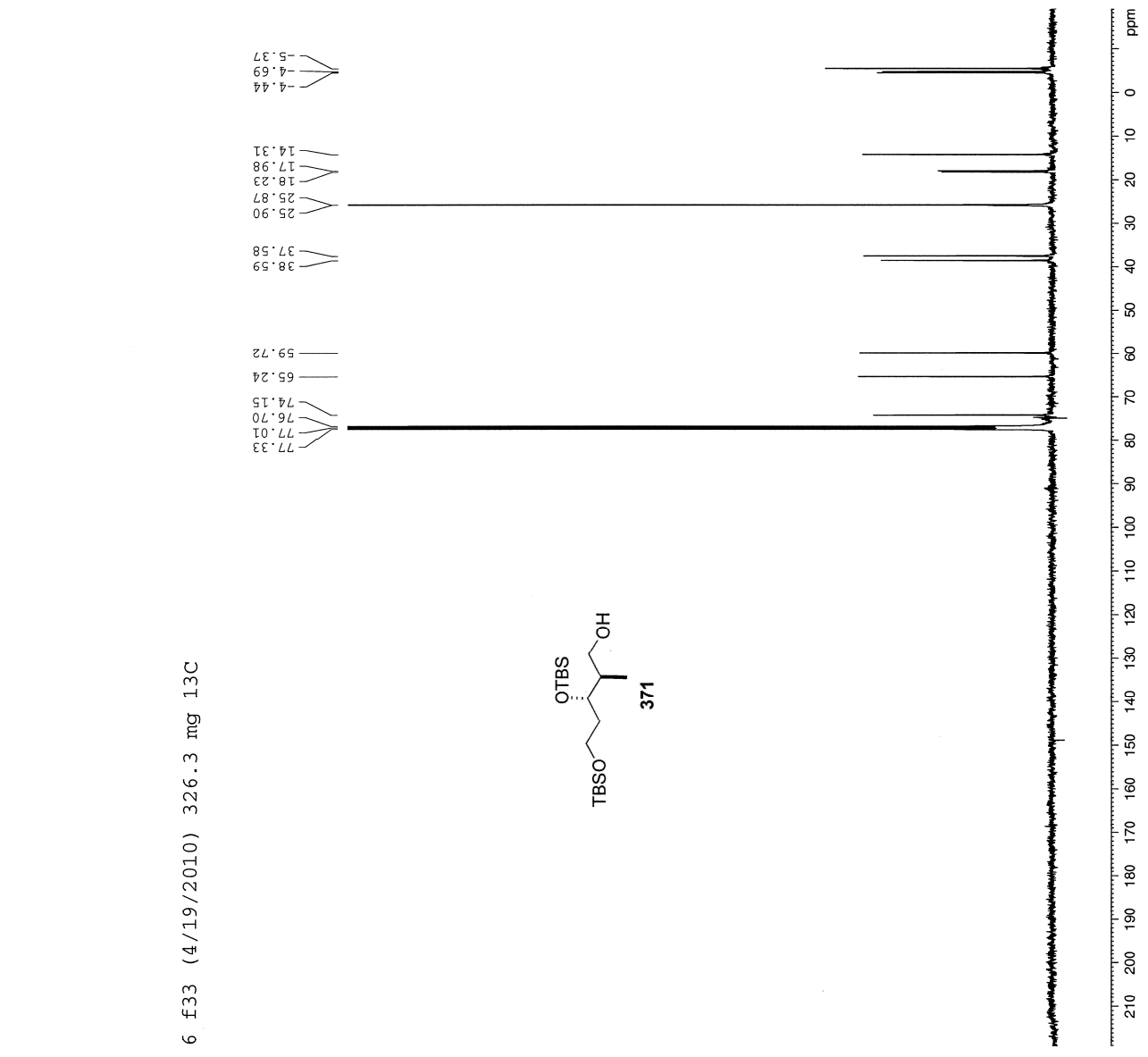

NAME ks-T04-57-1
EXPNO 2
PROCNO 1
Date_ 20100205
Time 14.09
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 90.5
DW 78.000 u
DE 6.50 u
TE 299.5 K
D1 1.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1378009 M
SI 32768
SF 400.1350000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
57 f3-10 (2/5/2010) 143.6 mg
367
ppm
1.00
1.34
1.34
1.17
1.57
5.12
4.21
0.28
3.34
1.09

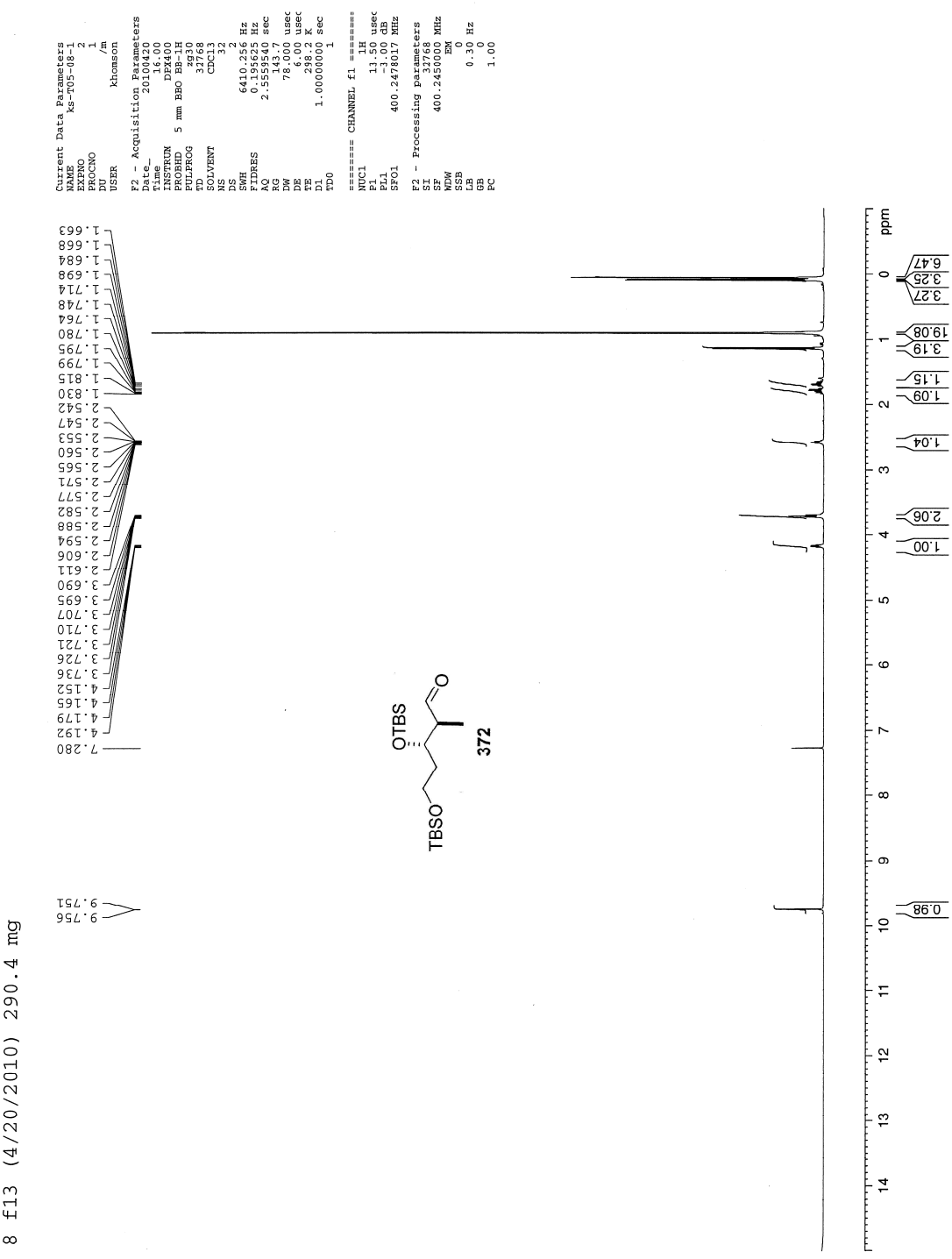

57 f3-10 (2/5/2010) 143.6 mg 13C
NAME ks-T04-57-1
EXPNO 8
PROCNO 1
Date_ 20100206
Time 7.33
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 1290.2
DW 20.850 u
DE 6.50 u
TE 301.8 K
D1 2.00000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
PL1W 46.89702606 W
SFO1 100.6240872 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1366005 M
SI 32768
SF 100.6140260 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
9.60
19.10
28.69
29.68
51.06
59.69
70.06
76.70
77.02
77.33
98.49
102.21
204.25
367
200
180
160
140
120
100
80
60
40
20
0
ppm

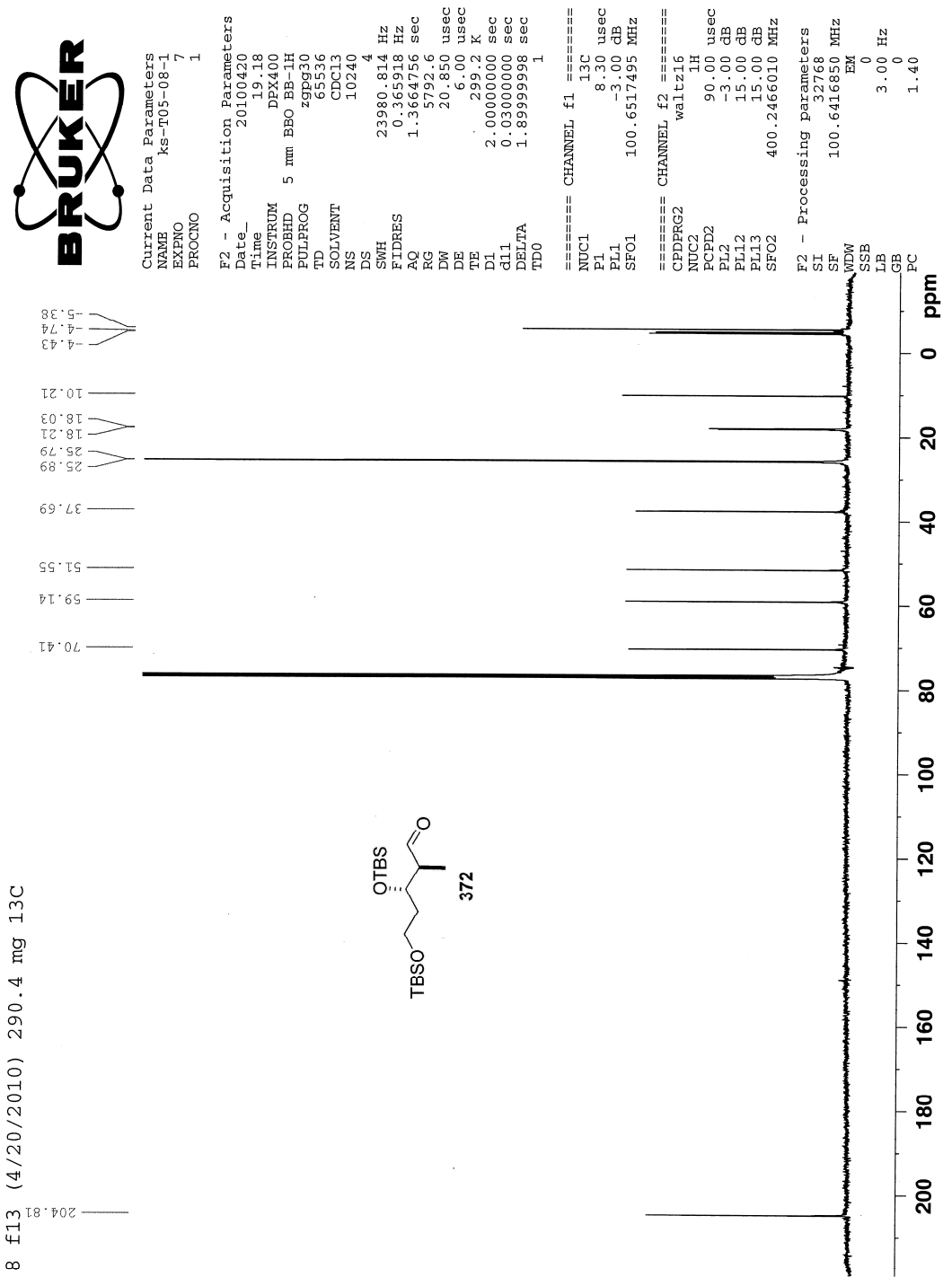

64 f5-6 (2/24/2010) 877.7 mg
Current Data Parameters
NAME ks-T04-64-1
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100224
Time 13.36
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 114
DW 78.000
DE 6.00
TE 298.2
D1 1.00000000
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50
PL1 -3.00
SFO1 400.2478017
F2 - Processing parameters
SI 32768
SF 400.2450000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
OTBS
TBSO
370
ppm

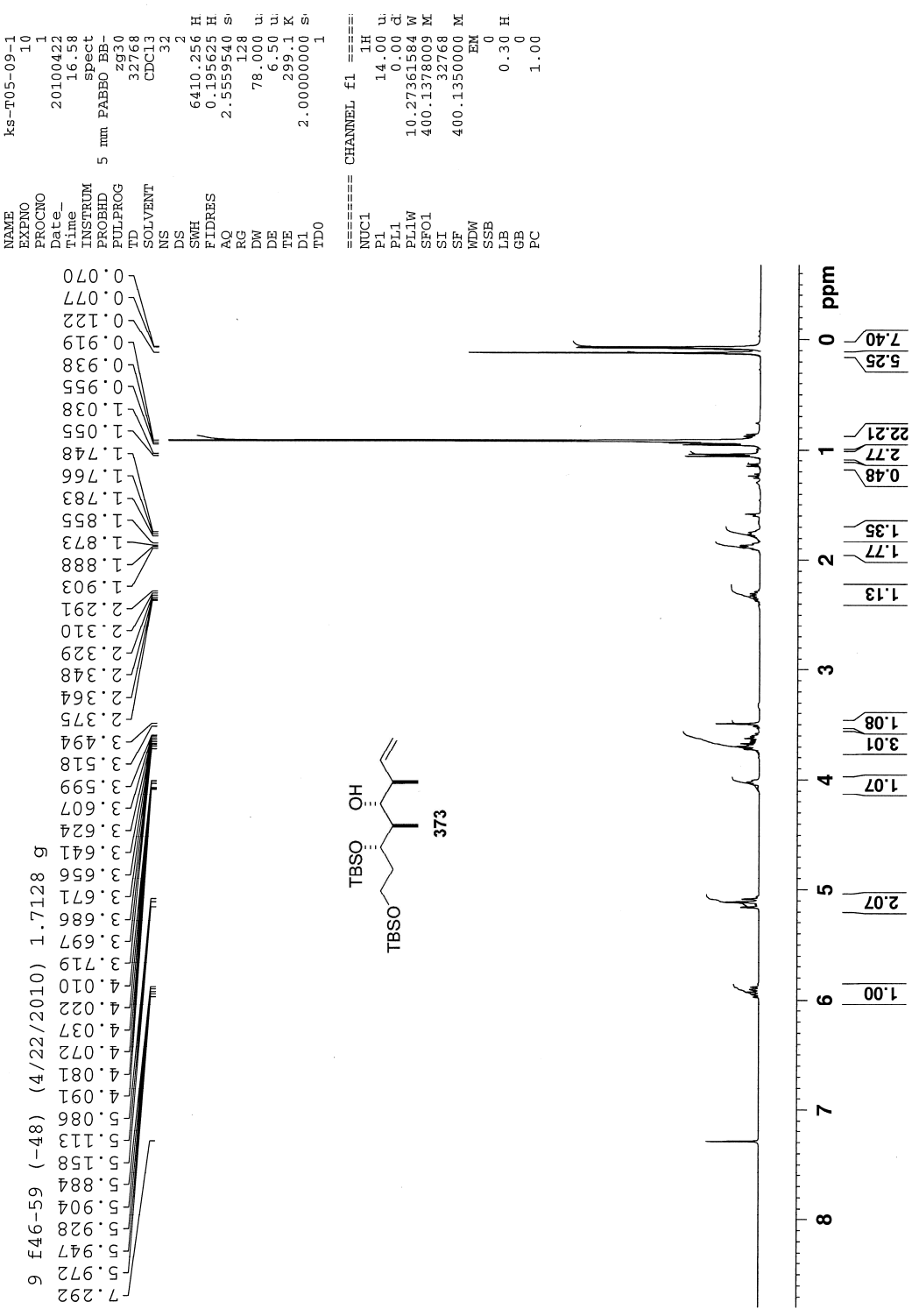

64 f5-6 (2/24/2010) 877.7 mg 13C
Current Data Parameters
NAME ks-T04-64-1
EXPNO 14
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100224
Time 15.28
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1927
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 6502
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OTBS
TBSO
370
ppm

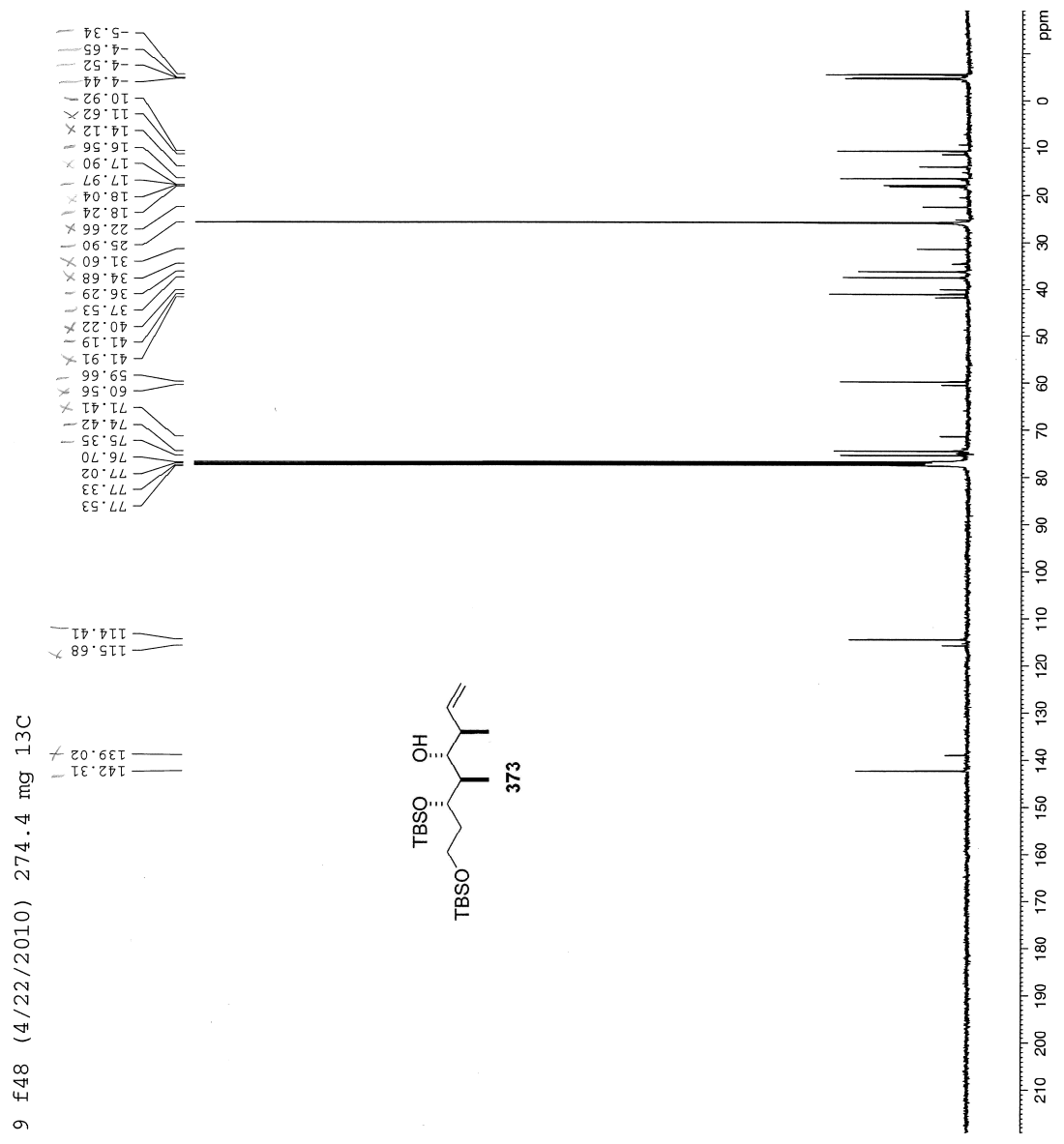

NAME ks-T05-06-1
EXPNO 2
PROCNO 1
Date_ 20100419
Time 16.27
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 71.8
DW 78.000 u
DE 6.50 u
TE 299.0 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1378009 M
SI 32768
SF 400.1350000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
6 f33 (4/19/2010) 326.3 mg
7.292
3.945
3.930
3.920
3.905
3.824
3.797
3.706
3.690
3.674
3.574
3.561
3.547
2.628
1.832
1.816
1.800
1.785
1.058
1.041
0.926
0.917
0.119
0.073
OTBS
TBSO
OH
371
ppm
7
6
5
4
3
2
1
0
1.00
0.98
2.02
1.01
0.89
2.91
3.09
8.85
8.65
5.92
5.82

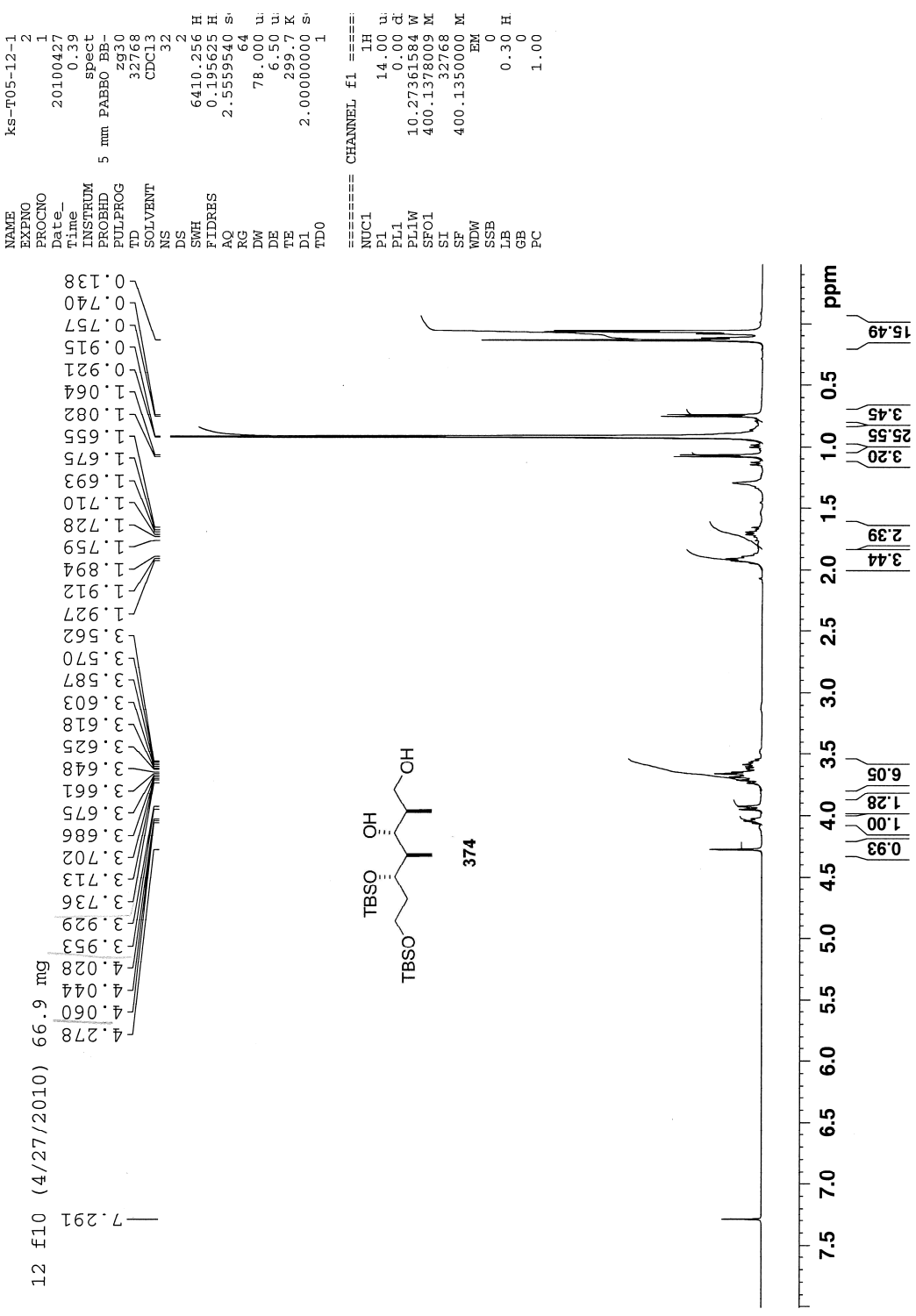

6 f33 (4/19/2010) 326.3 mg 13C
Current Data Parameters
NAME ks-705-06-1
EXPNO 9
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20100419
Time 19.51
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3096
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664735 sec
RG 7298.2
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
77.33
77.01
76.70
74.15
65.24
59.72
38.59
37.58
25.90
25.87
18.23
17.98
14.31
-4.44
-4.69
-5.37
OTBS
OH
TBSO
371
ppm


8 f13 (4/20/2010) 290.4 mg
Current Data Parameters
NAME Ks-T03-08-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20100420
Time 14.00
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195655 Hz
AQ 2.555540 sec
RG 143.7
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTBS
TBSO
O
372
ppm
6.47
3.27
3.25
3.19
19.08
1.15
1.09
1.04
2.06
1.00
0.98

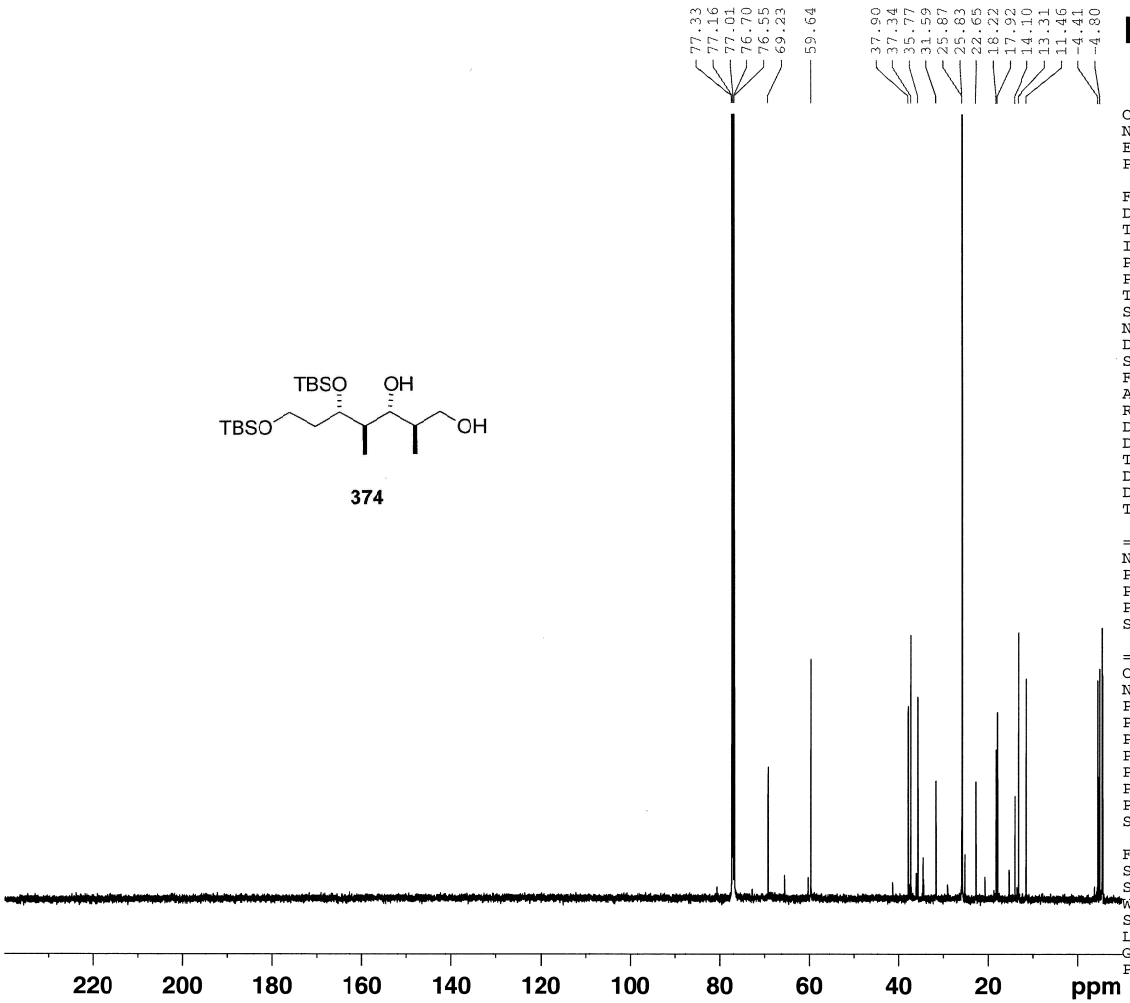

8 f13 (4/20/2010) 290.4 mg 13C
Current Data Parameters
NAME ks-T05-08-1
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100420
Time 19.18
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 5792.6
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
204.81
70.41
59.14
51.55
37.69
25.89
25.79
18.21
18.03
10.21
-4.43
-4.74
-5.38
OTBS
TBSO
O
372
200
180
160
140
120
100
80
60
40
20
0
ppm


NAME ks-T05-09-1
EXPNO 10
PROCNO 1
Date_ 20100422
Time_ 16.58
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.5559540 s
RG 128
DW 78.000 u
DE 6.50 u
TE 299.1 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1378009 M
SI 32768
SF 400.1350000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
9 f46-59 (-48) (4/22/2010) 1.7128 g
TBSO
OH
TBSO
373
ppm
7.40
5.25
22.21
2.77
0.48
1.35
1.77
1.13
1.08
3.01
1.07
2.07
1.00


9 f48 (4/22/2010) 274.4 mg 13C
Current Data Parameters
NAME ks-T05-09-1
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100422
Time 16.54
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4032
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 18390.4
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
142.31
139.02
115.68
114.41
77.53
77.33
77.02
76.70
75.35
74.42
71.41
60.56
59.66
41.91
41.19
40.22
37.53
36.29
34.68
31.60
25.90
22.66
18.24
18.04
17.97
17.90
16.56
14.12
11.62
10.92
-4.44
-4.52
-4.65
-5.34
TBSO
OH
TBSO
373
ppm


NAME ks-T05-12-1
EXPNO 2
PROCNO 1
Date_ 20100427
Time 0.39
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 H
FIDRES 0.195625 H
AQ 2.55595540 s
RG 64
DW 78.000 u
DE 6.50 u
TE 299.7 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1W 10.27361584 W
SFO1 400.1378009 M
SI 32768
SF 400.1350000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
12 f10 (4/27/2010) 66.9 mg
7.291
4.278
4.060
4.044
4.028
3.953
3.929
3.736
3.713
3.702
3.686
3.675
3.661
3.648
3.625
3.618
3.603
3.587
3.570
3.562
1.927
1.912
1.894
1.759
1.728
1.710
1.693
1.675
1.655
1.082
1.064
0.921
0.915
0.757
0.740
0.138
TBSO
OH
OH
TBSO
374
ppm
15.49
3.45
25.55
3.20
3.44
2.39
6.05
1.28
1.00
0.93

12 f10 (4/27/2010) 66.9 mg 13C



374

BRUKER

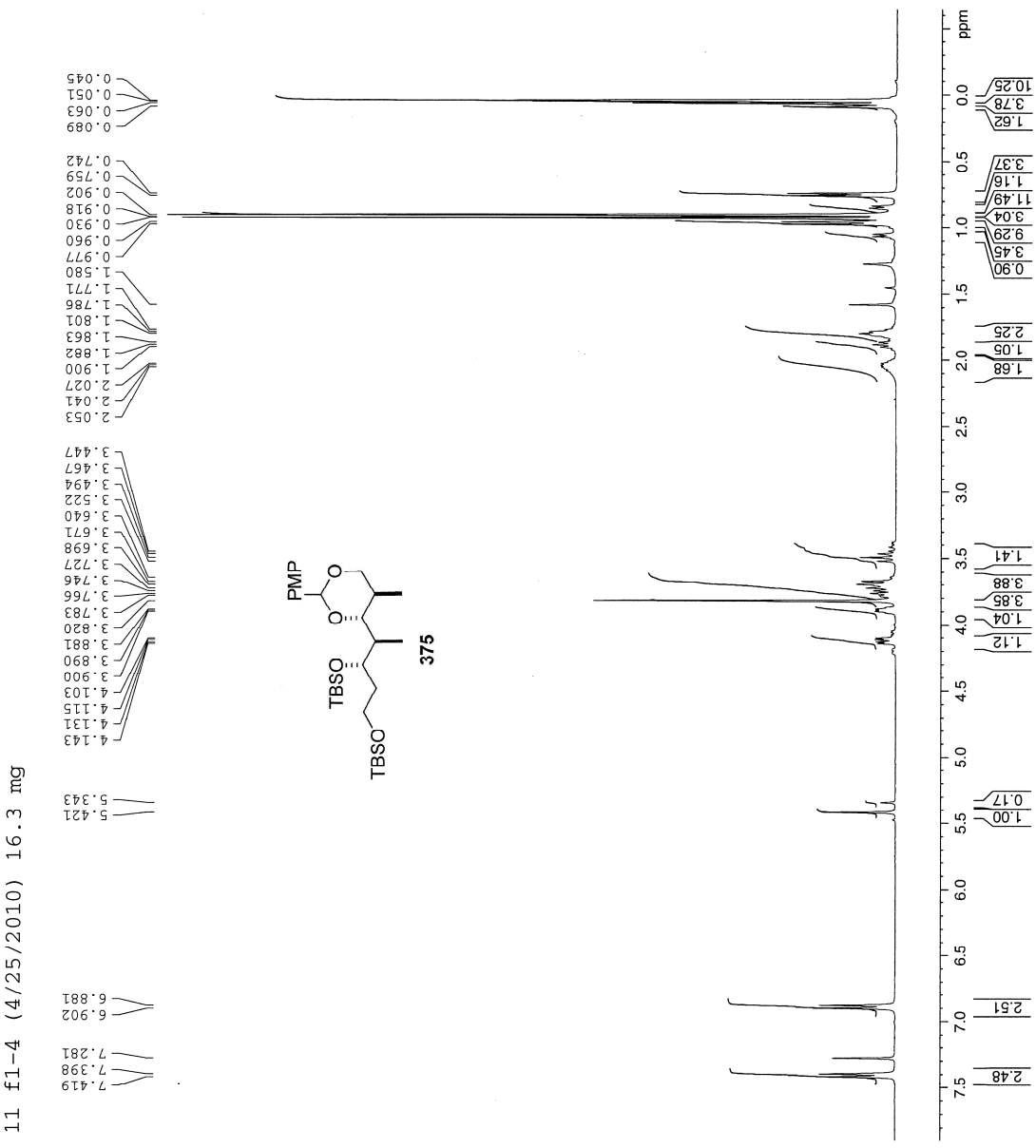
Current Data Parameters
NAME ks-T05-12-1
EXPNO 10
PROCNO 1

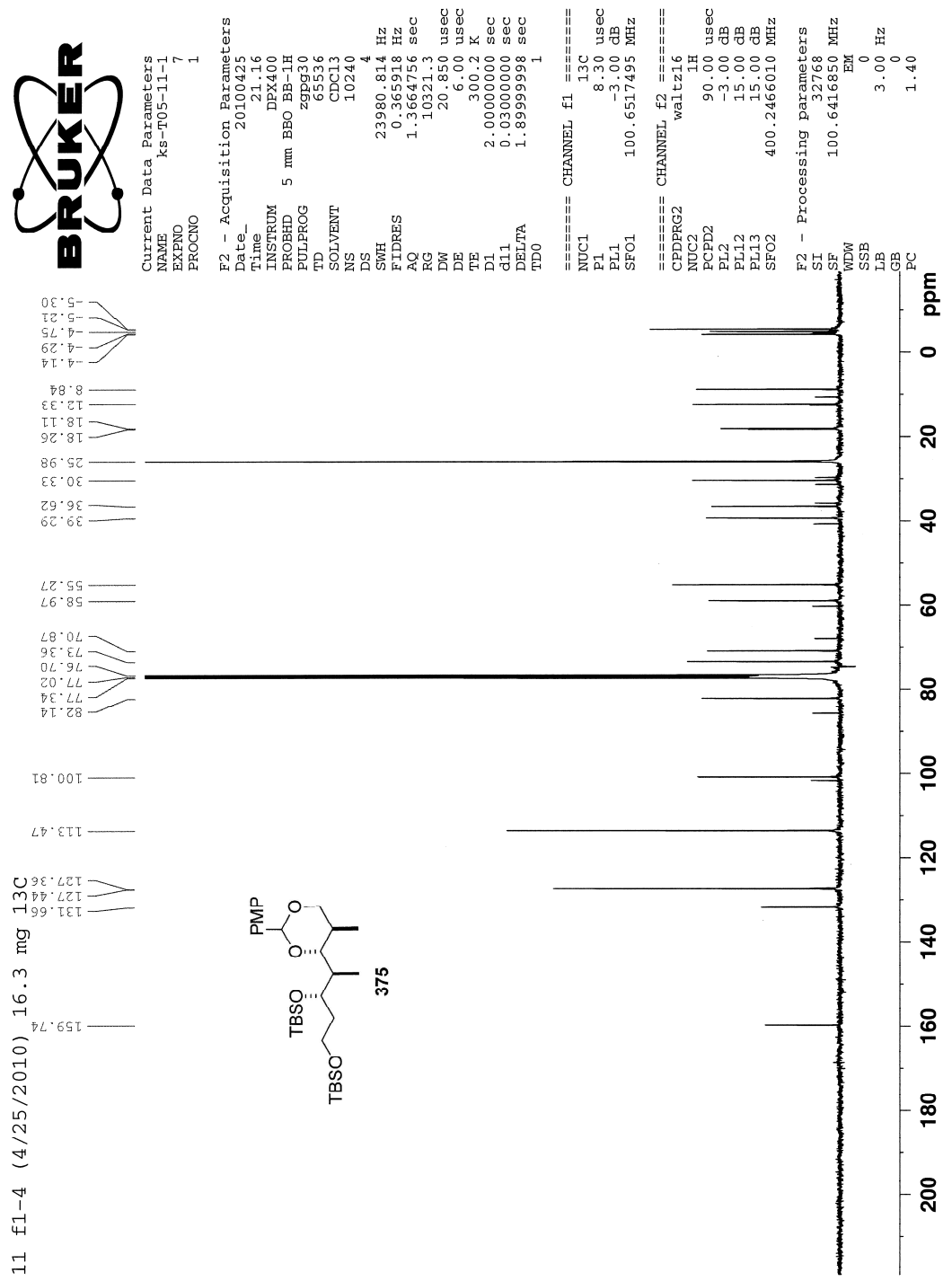
F2 - Acquisition Parameters
Date_ 20100427
Time 8.30
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4146
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.50 usec
TE 300.9 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

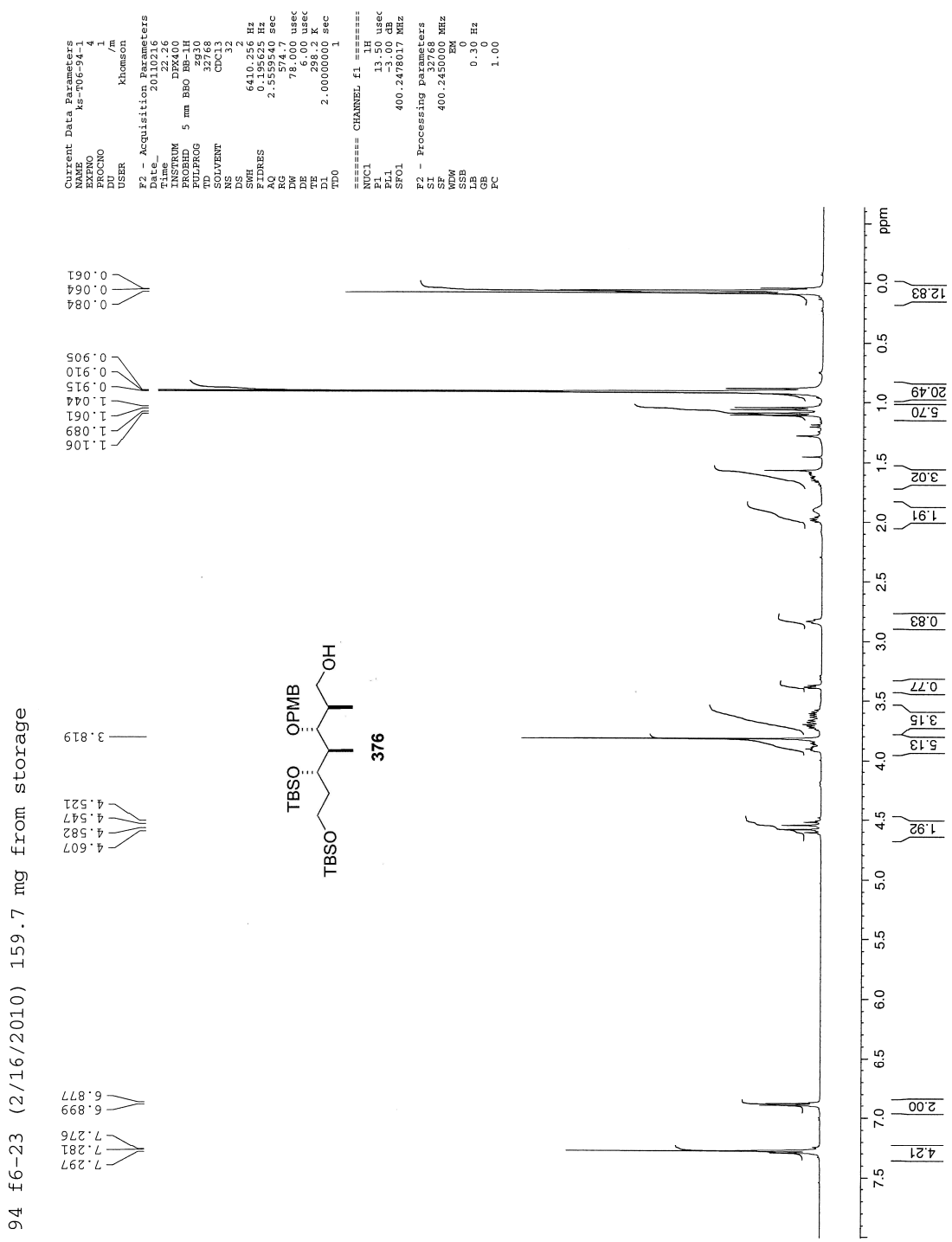
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 -2.00 dB
PL1W 46.89702606 W
SFO1 100.6255966 MHz

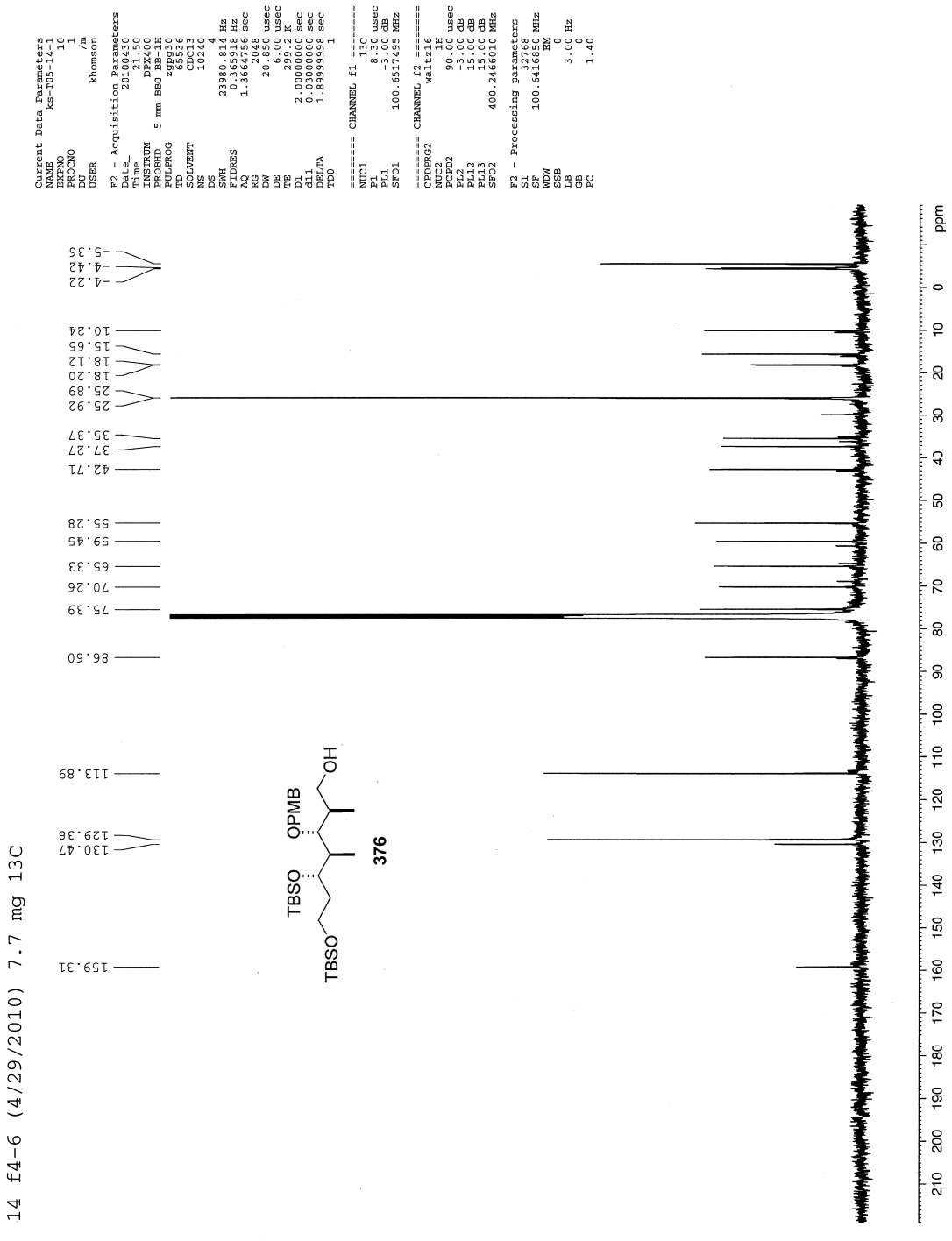
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 16.16 dB
PL13 17.00 dB
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1366005 MHz

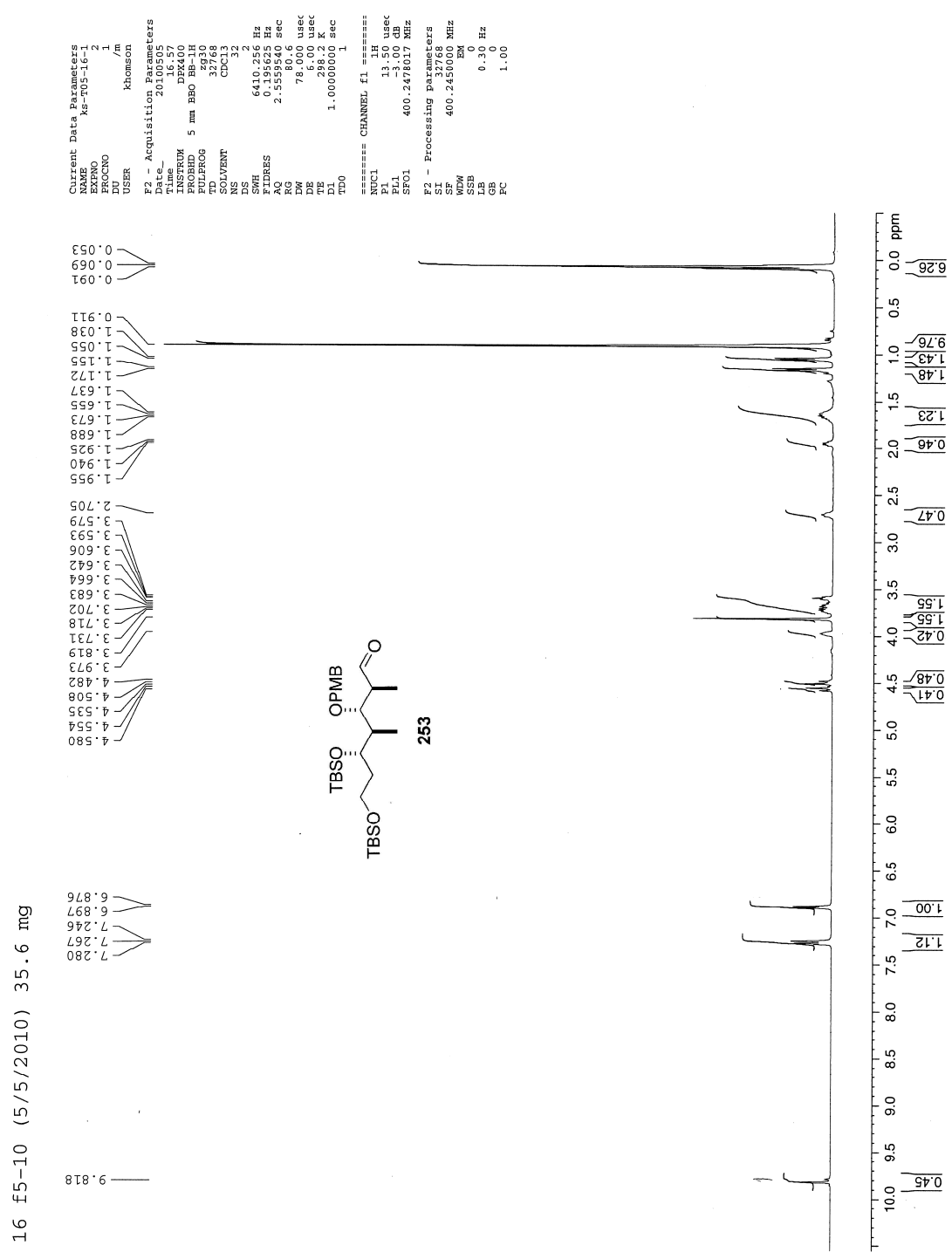
F2 - Processing parameters
SI 32768
SF 100.6140260 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

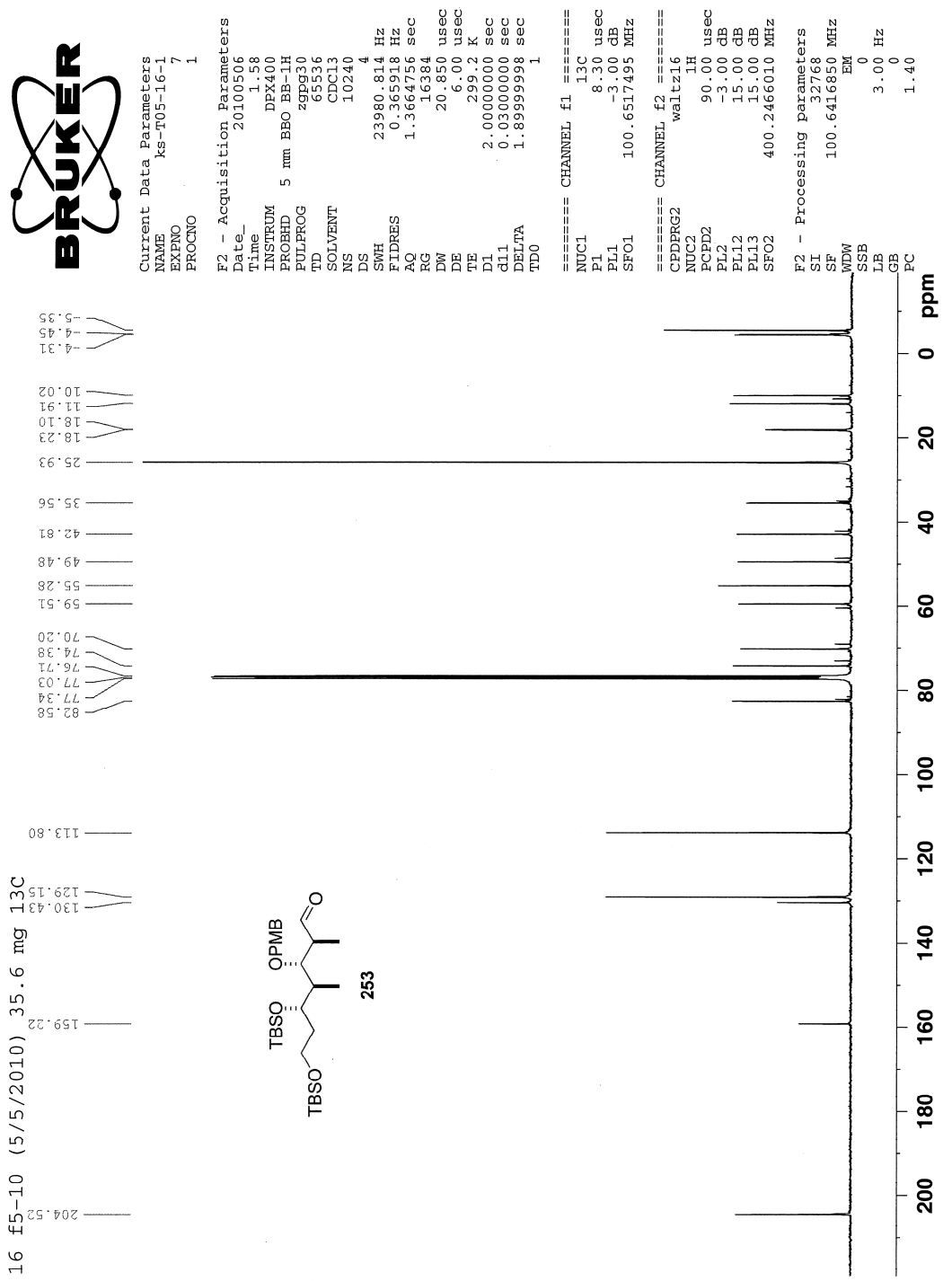

11 f1-4 (4/25/2010) 16.3 mg
Current Data Parameters
NAME ks-705-11-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
P2 - Acquisition Parameters
Date_ 20100425
Time 14.43
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55595540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
PMP
TBSO
TBSO
375
ppm

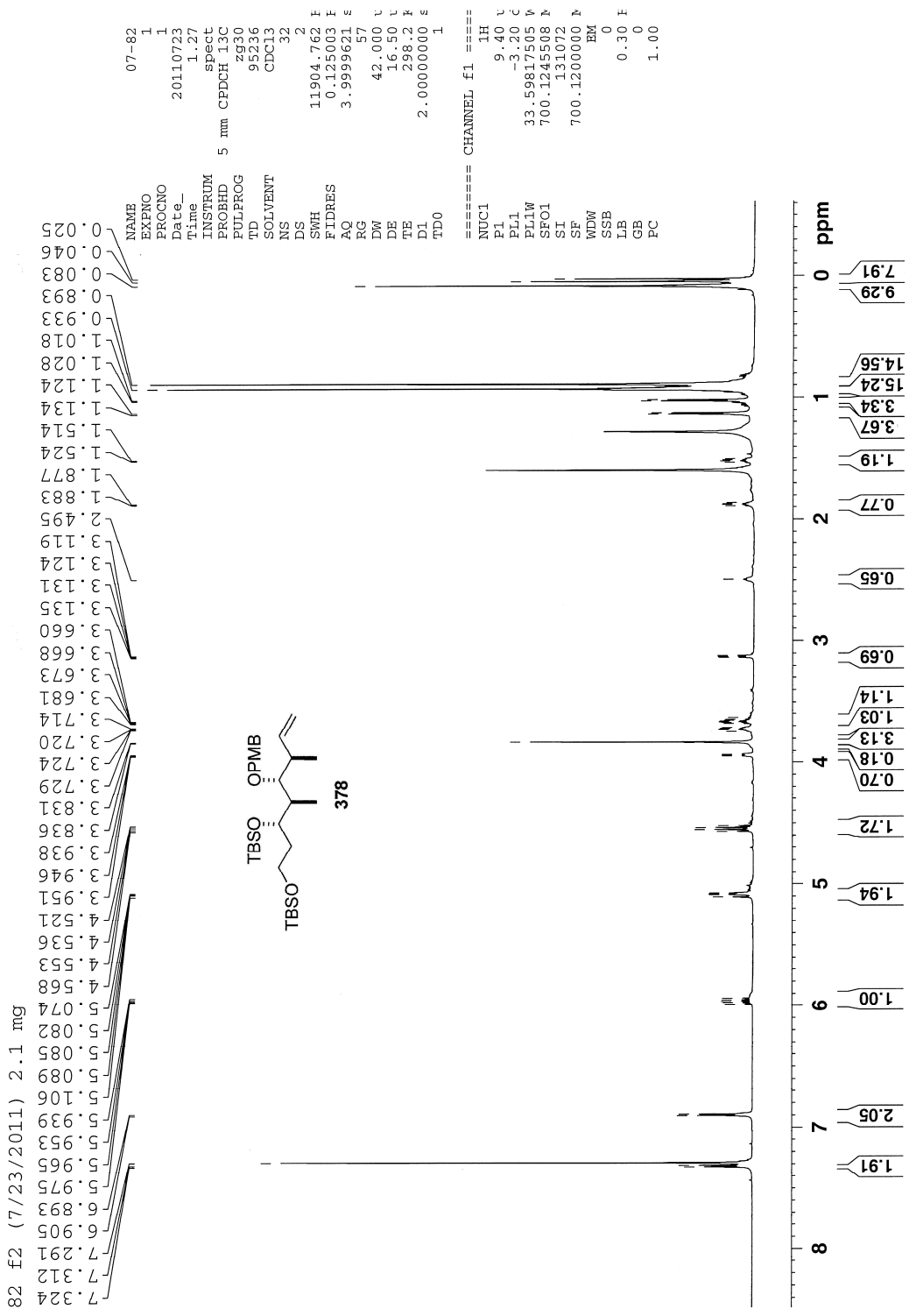

11 f1-4 (4/25/2010) 16.3 mg 13C
Current Data Parameters
NAME ks-T05-11-1
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100425
Time 21.16
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 10321.3
DW 20.850 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
-5.30
-5.21
-4.75
-4.29
-4.14
8.84
12.33
18.11
18.26
25.98
30.33
36.62
39.29
55.27
58.97
70.87
73.36
76.70
77.02
77.34
82.14
100.81
113.47
127.36
127.44
131.66
159.74
PMP
TBSO
TBSO
375
ppm
200
180
160
140
120
100
80
60
40
20
0

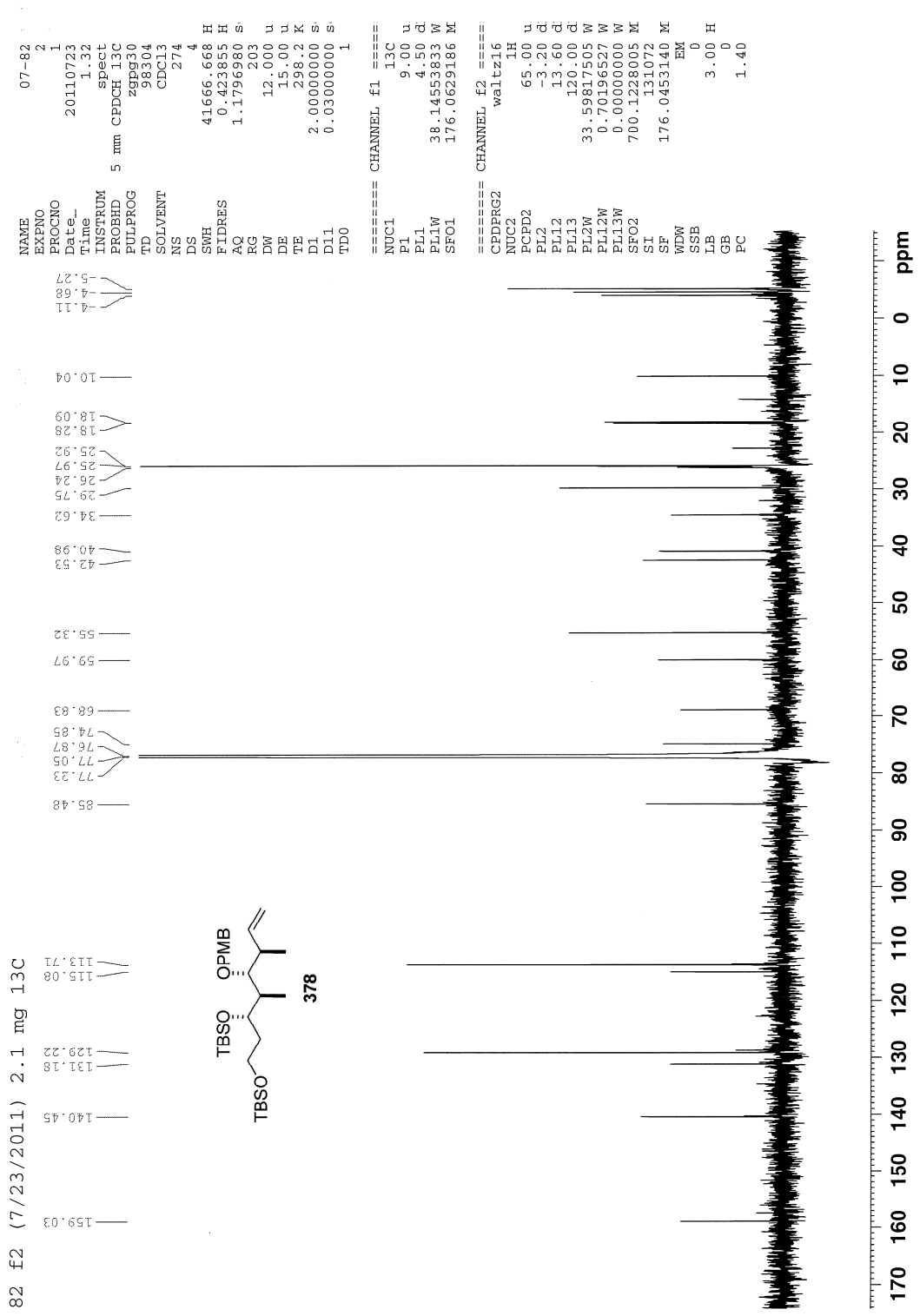

94 f6-23 (2/16/2010) 159.7 mg from storage
Current Data Parameters
NAME ks-706-94-1
EXPNO 4
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20110216
Time_ 22.26
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 574.7
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TBSO
OPMB
OH
TBSO
376
ppm

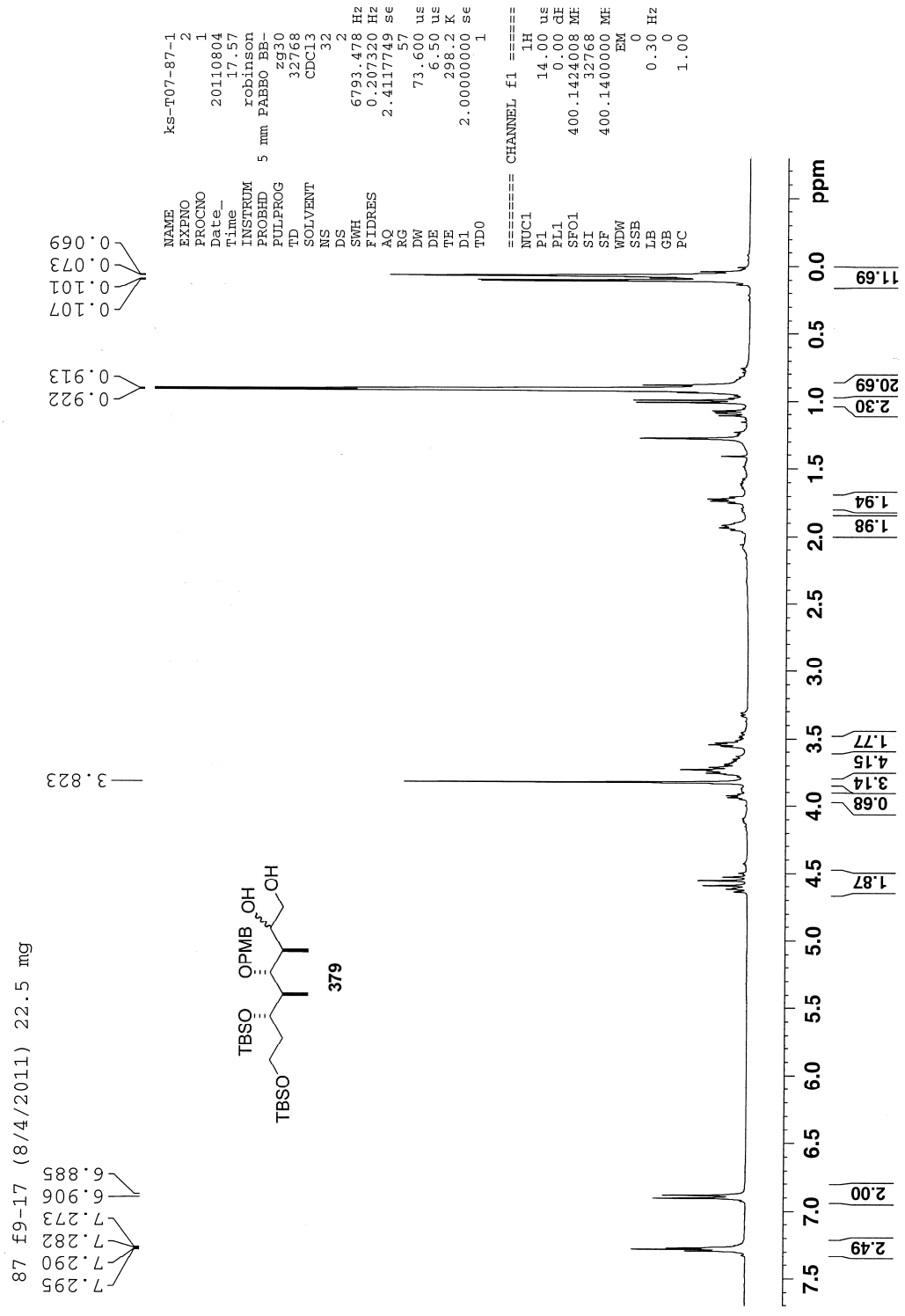

14 f4-6 (4/29/2010) 7.7 mg 13C
Current Data Parameters
NAME ks-T05-14-1
EXPNO 10
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20100430
Time 21.50
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.36664756 sec
RG 20048
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
-5.36
-4.42
-4.22
10.24
15.65
18.12
18.20
25.89
25.92
35.37
37.27
42.71
55.28
59.45
65.33
70.26
75.39
86.60
113.89
129.38
130.47
159.31
TBSO
OPMB
TBSO
OH
376
ppm

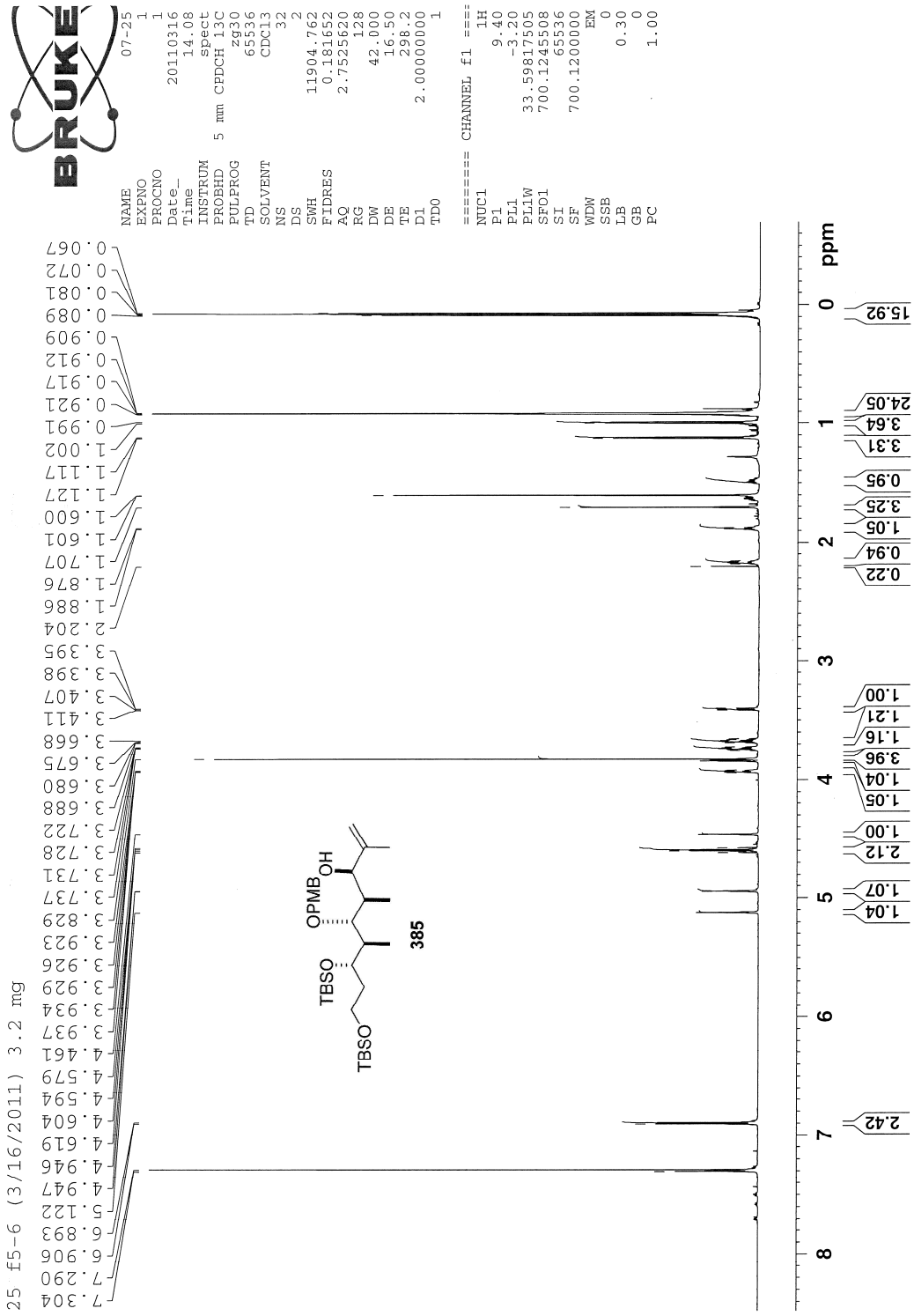

16 f5-10 (5/5/2010) 35.6 mg
Current Data Parameters
NAME ks-T05-16-1
EXPNO 2
PROCNO 1
DU /m
USER khomson
F2 - Acquisition Parameters
Date_ 20100505
Time 16.57
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55559540 sec
RG 80.6
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TBSO
OPMB
TBSO
O
253
9.818
7.280
7.267
7.246
6.897
6.876
4.580
4.554
4.535
4.508
4.482
3.973
3.819
3.731
3.718
3.702
3.683
3.664
3.642
3.606
3.593
3.579
2.705
1.955
1.940
1.925
1.688
1.673
1.655
1.637
1.172
1.155
1.055
1.038
0.911
0.091
0.069
0.053
6.26
9.76
1.43
1.48
1.23
0.46
0.47
1.55
1.55
0.42
0.48
0.41
1.00
1.12
0.45
ppm

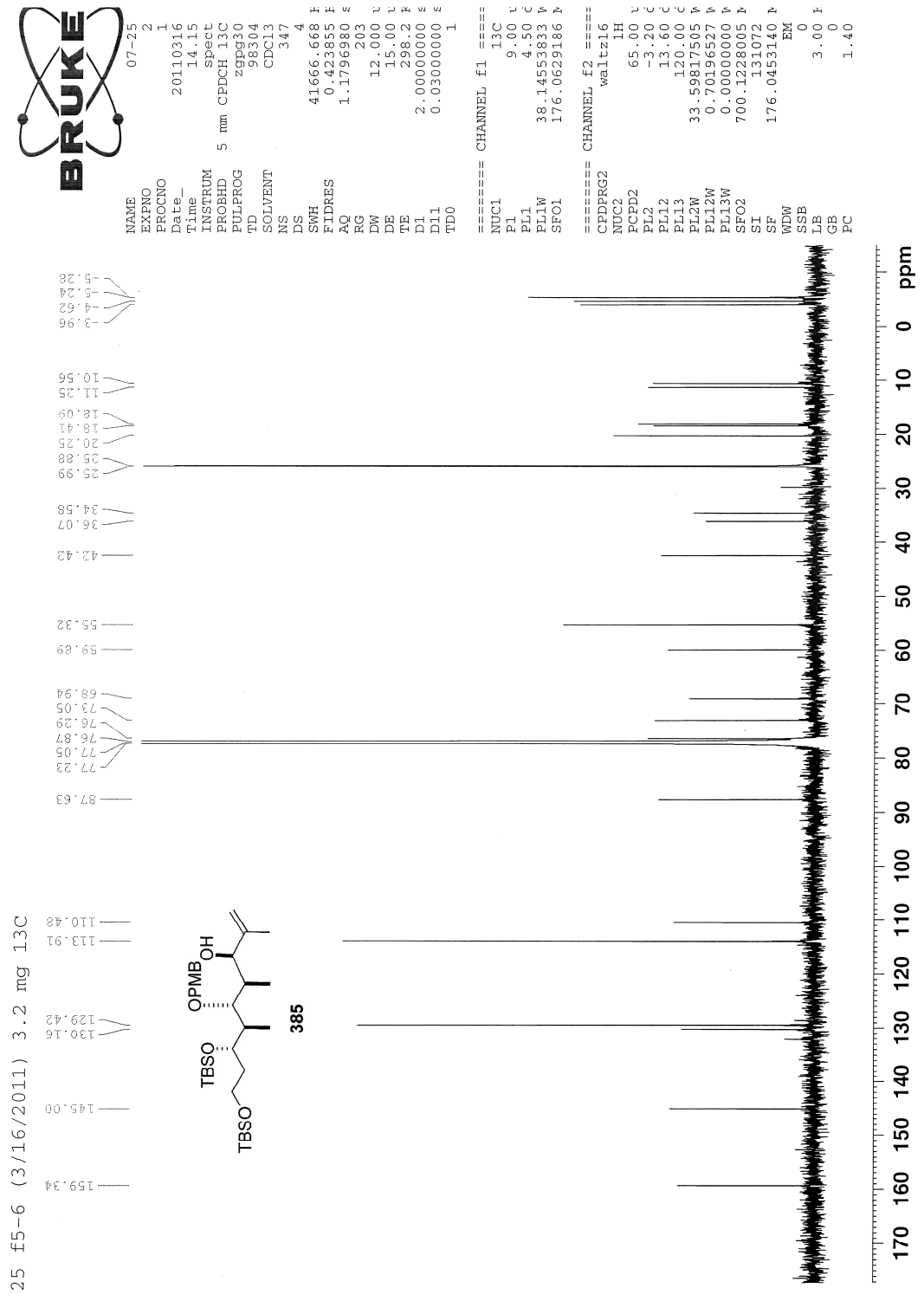

16 f5-10 (5/5/2010) 35.6 mg 13C
Current Data Parameters
NAME ks-T05-16-1
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100506
Time 1.58
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
TBSO
OPMB
TBSO
O
253
204.52
159.22
130.43
129.15
113.80
82.58
77.34
77.03
76.71
74.38
70.20
59.51
55.28
49.48
42.81
35.56
25.93
18.23
18.10
11.91
10.02
-4.31
-4.45
-5.35
200
180
160
140
120
100
80
60
40
20
0
ppm

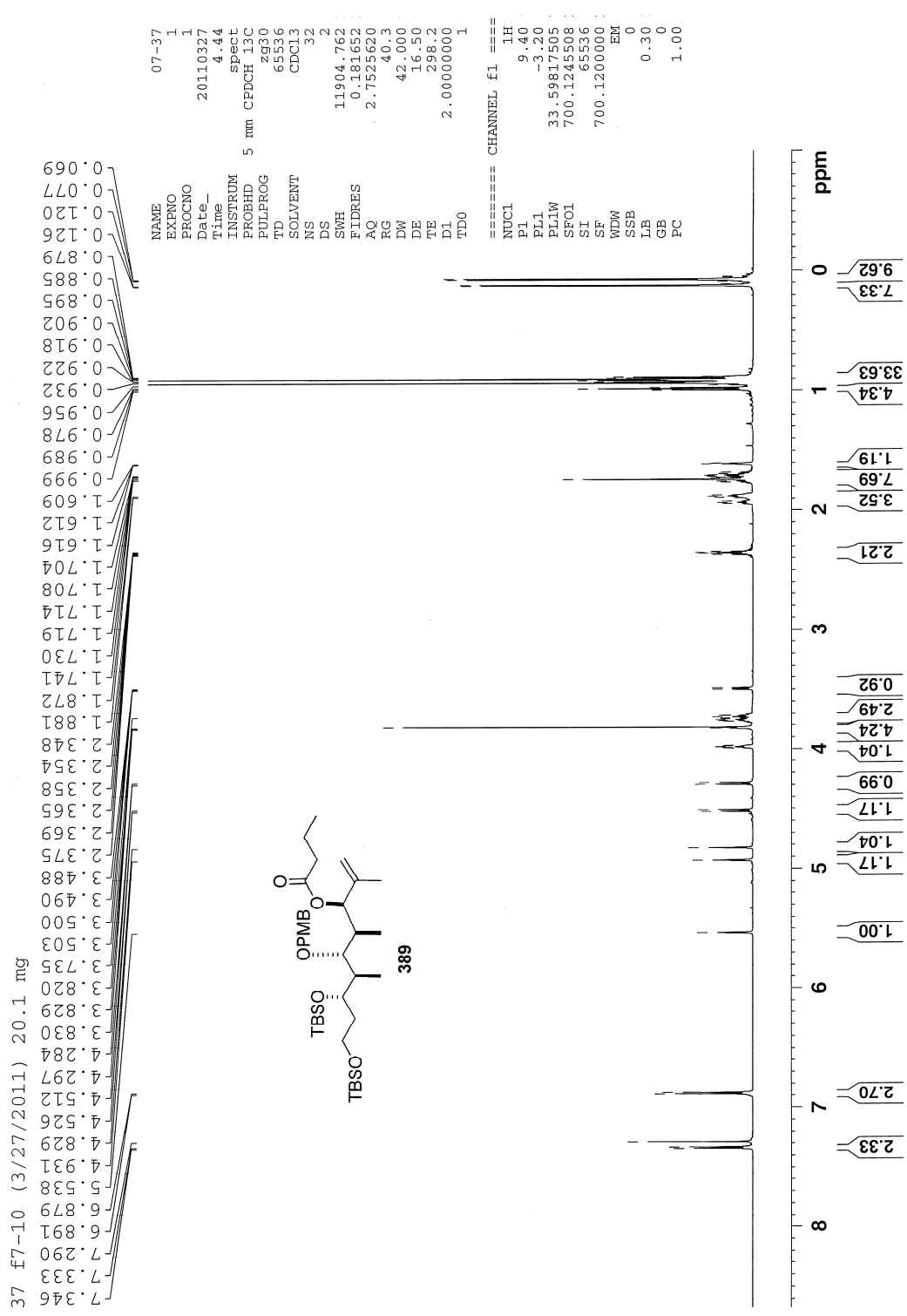

TBSO
OPMB
TBSO
378
ppm

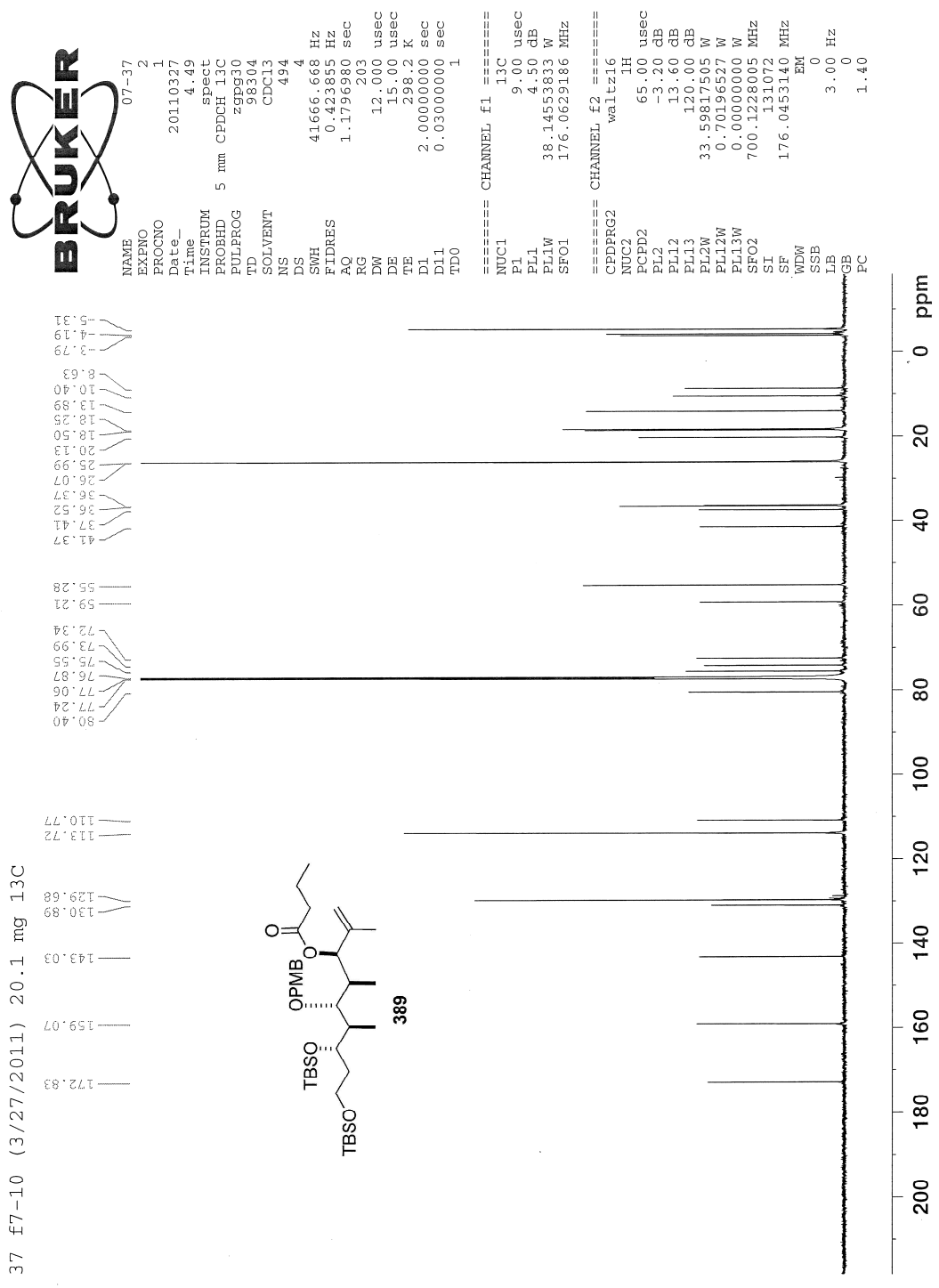

82 f2 (7/23/2011) 2.1 mg 13C
TBSO
OPMB
TBSO
378
NAME 07-82
EXPNO 2
PROCNO 1
Date_ 20110723
Time_ 1.32
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDC13
NS 274
DS 4
SWH 41666.668 H
FIDRES 0.423855 H
AQ 1.1796980 s
RG 203
DW 12.000 u
DE 15.00 u
TE 298.2 K
D1 2.00000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 9.00 u
PL1 4.50 d
PL1W 38.14553833 W
SFO1 176.0629186 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 u
PL2 -3.20 d
PL12 13.60 d
PL13 120.00 d
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 M
SI 131072
SF 176.0453140 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
-5.27
-4.68
-4.11
10.04
18.09
18.28
25.92
25.97
26.24
29.75
34.62
40.98
42.53
55.32
59.97
68.83
74.85
76.87
77.05
77.23
85.48
113.71
115.08
129.22
131.18
140.45
159.03
ppm

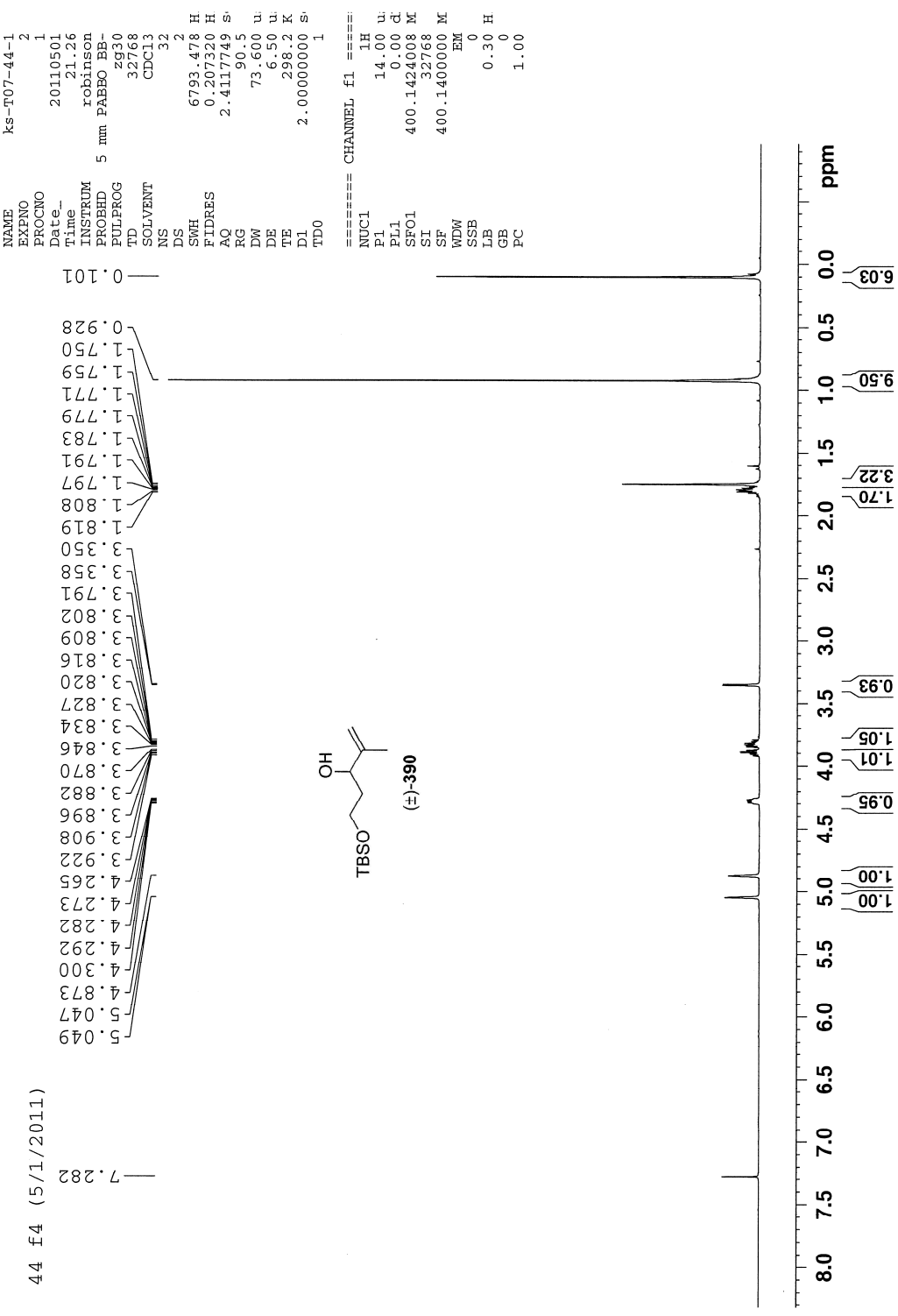

87 f9-17 (8/4/2011) 22.5 mg
379
TBSO
OPMB
OH
TBSO
OH
ppm

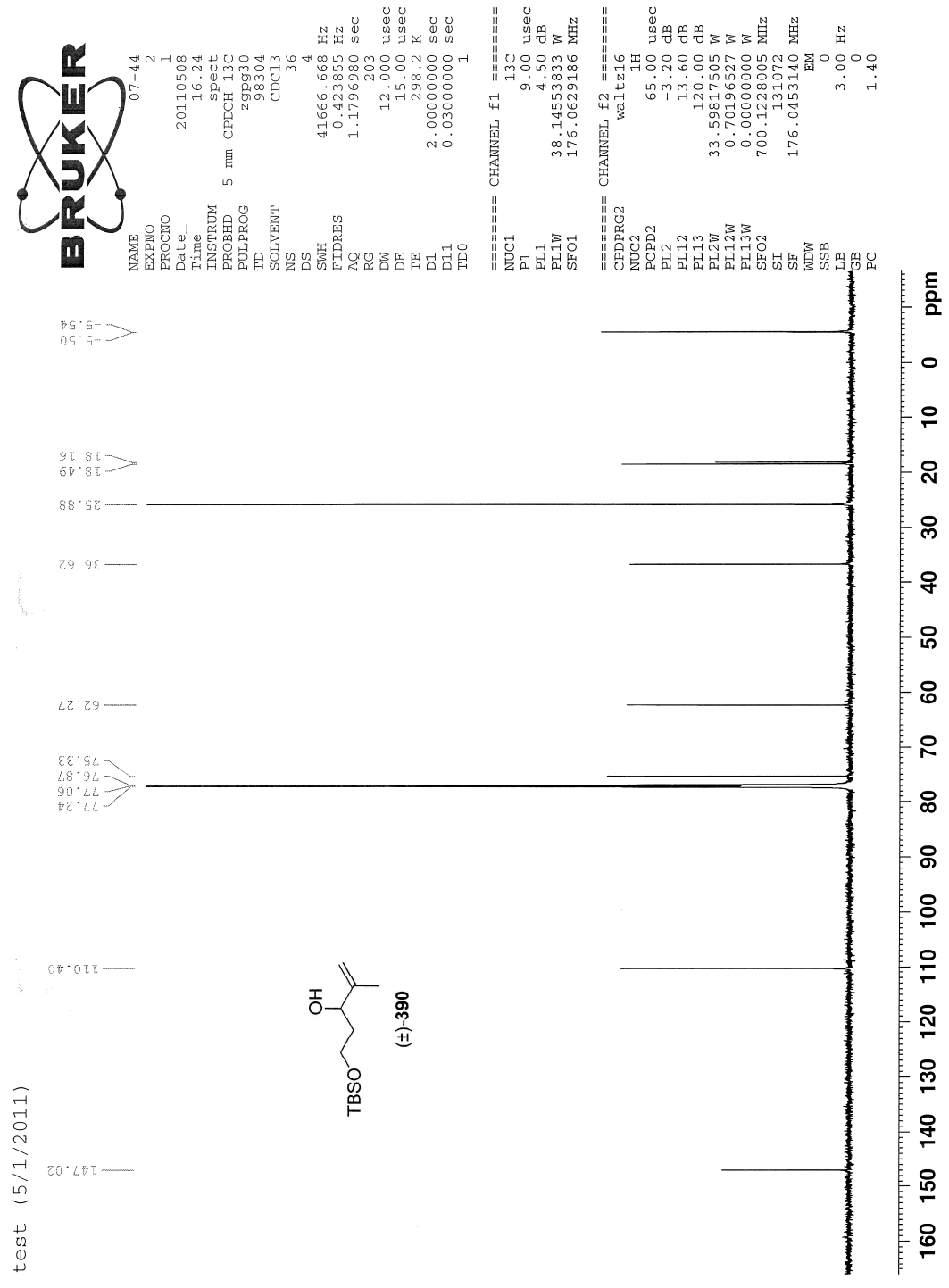

25 f5-6 (3/16/2011) 3.2 mg
NAME 07-25
EXPNO 1
PROCNO 1
Date_ 20110316
Time 14.08
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762
FIDRES 0.181652
AQ 2.7525620
RG 128
DW 42.000
DE 16.50
TE 298.2
D1 2.00000000
TDO 1
======== CHANNEL f1 ====
NUC1 1H
P1 9.40
PL1 -3.20
PL1W 33.59817505
SFO1 700.1245508
SI 65536
SF 700.1200000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
TBSO
OPMB
OH
TBSO
385
ppm

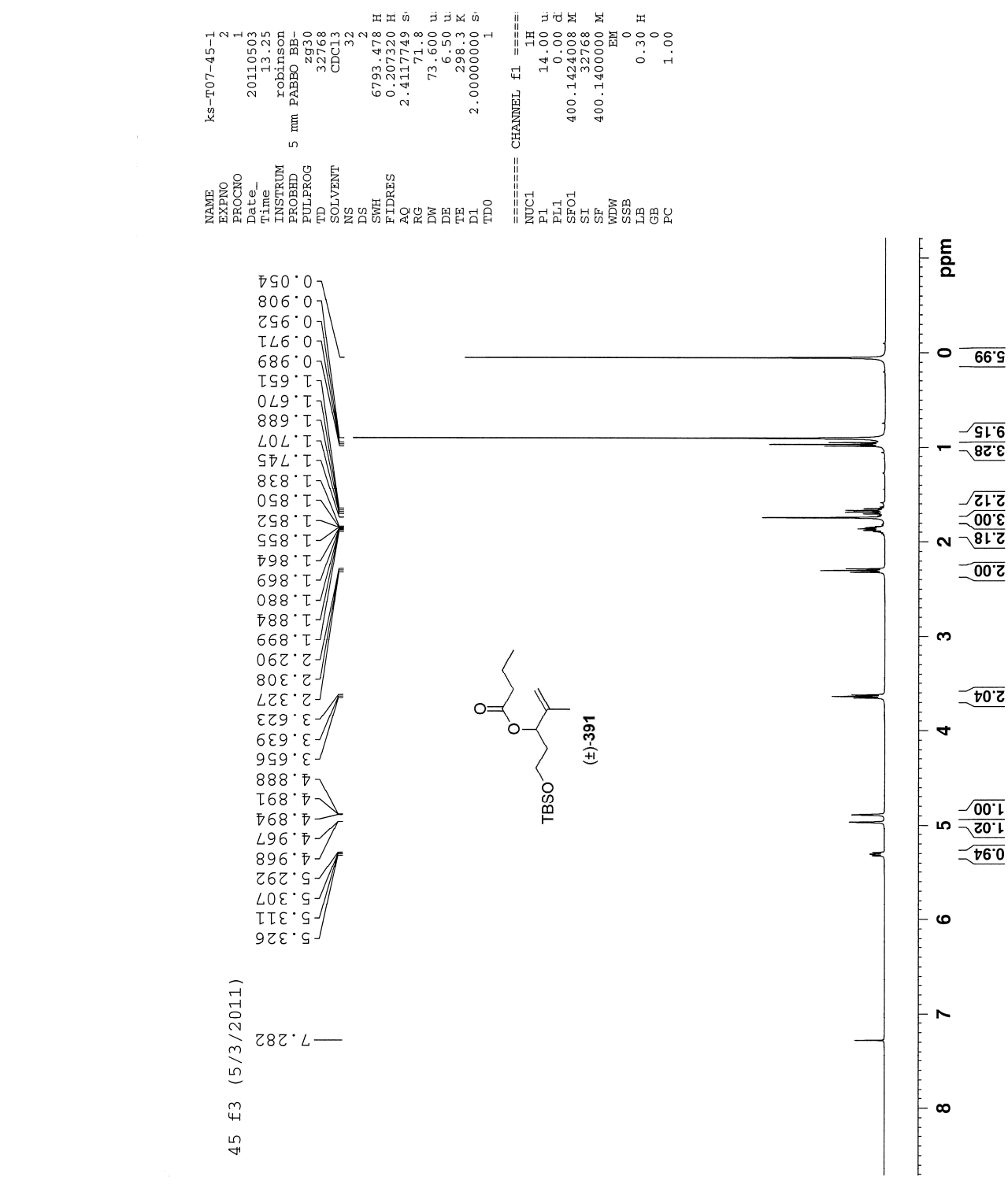

25 f5-6 (3/16/2011) 3.2 mg 13C
385
TBSO
OPMB
OH
TBSO
ppm


37 f7-10 (3/27/2011) 20.1 mg
NAME 07-37
EXPNO 1
PROCNO 1
Date_ 20110327
Time 4.44
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762
FIDRES 0.181652
AQ 2.7525620
RG 40.3
DW 42.000
DE 16.50
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 9.40
PL1 -3.20
PL1W 33.59817505
SFO1 700.1245508
SI 65536
SF 700.1200000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
OPMB
TBSO
TBSO
O
O
389
ppm
9.62
7.33
33.63
4.34
1.19
7.69
3.52
2.21
0.92
2.49
4.24
1.04
0.99
1.17
1.04
1.17
1.00
2.70
2.33

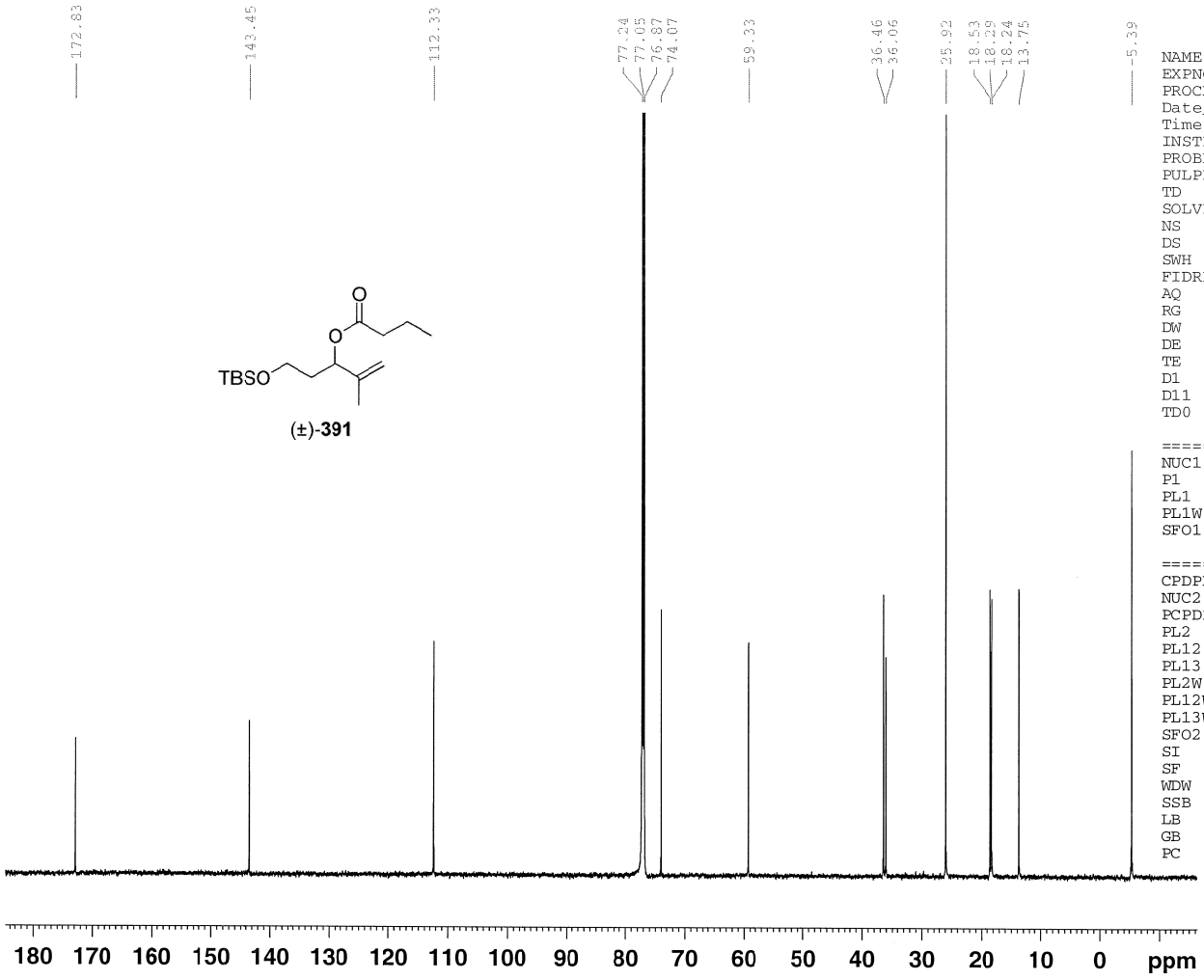

37 f7-10 (3/27/2011) 20.1 mg 13C
NAME 07-37
EXPNO 2
PROCNO 1
Date_ 20110327
Time 4.49
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDC13
NS 494
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OPMB
TBSO
TBSO
389
ppm


NAME ks-T07-44-1
EXPNO 2
PROCNO 1
Date_ 20110501
Time 21.26
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 90.5
DW 73.600 u
DE 6.50 u
TE 298.2 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
44 f4 (5/1/2011)
7.282
5.049
5.047
4.873
4.300
4.292
4.282
4.273
4.265
3.922
3.908
3.896
3.882
3.870
3.846
3.834
3.827
3.820
3.816
3.809
3.802
3.791
3.358
3.350
1.819
1.808
1.797
1.791
1.783
1.779
1.771
1.759
1.750
0.928
0.101
TBSO
OH
(±)-390
ppm
6.03
9.50
3.22
1.70
0.93
1.05
1.01
0.95
1.00
1.00

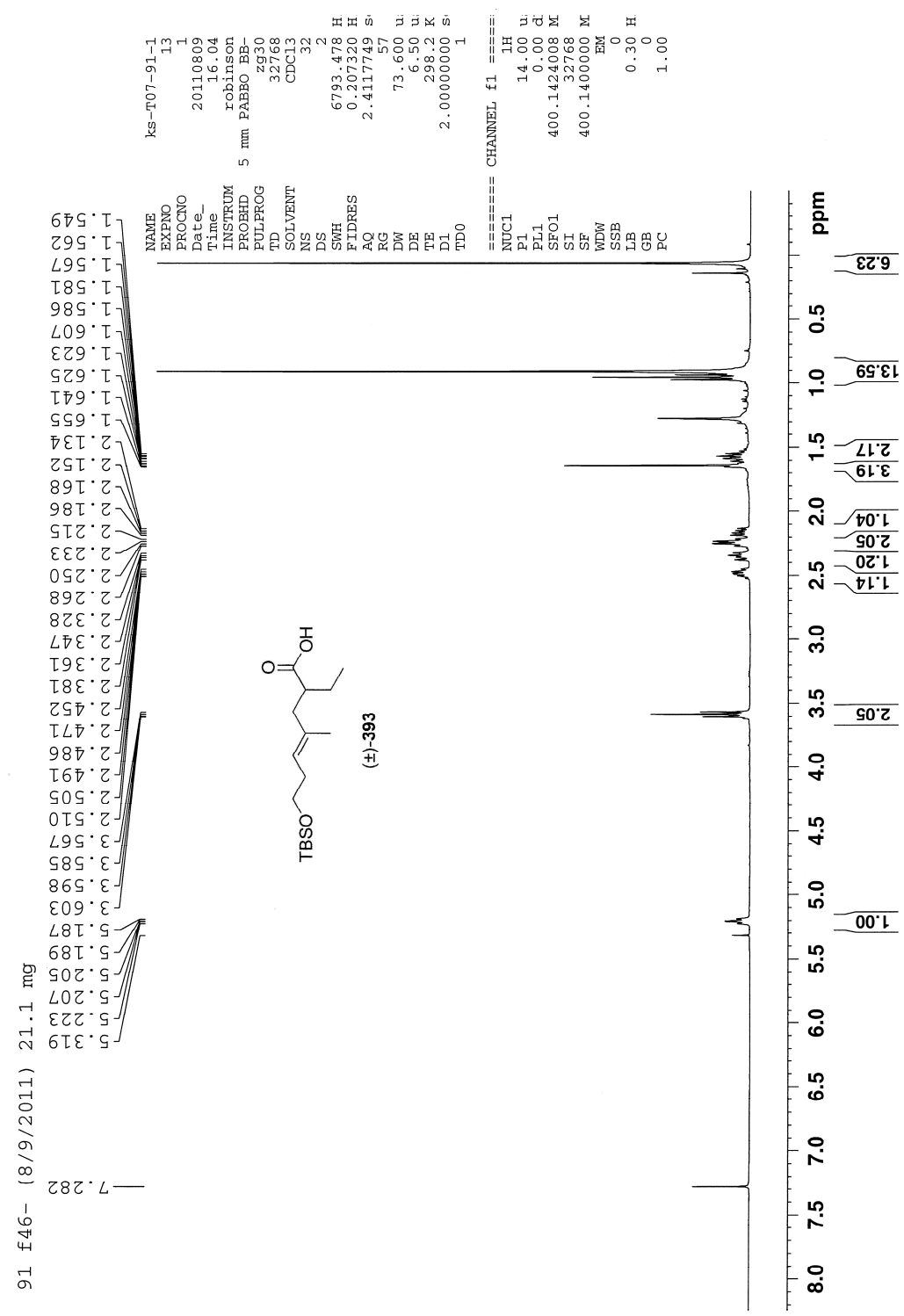

test (5/1/2011)
BRUKER
NAME 07-44
EXPNO 2
PROCNO 1
Date_ 20110508
Time_ 16.24
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDC13
NS 36
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
-5.54
-5.50
18.16
18.49
25.88
36.62
62.27
75.33
76.87
77.06
77.24
110.40
147.02
OH
TBSO
(±)-390
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

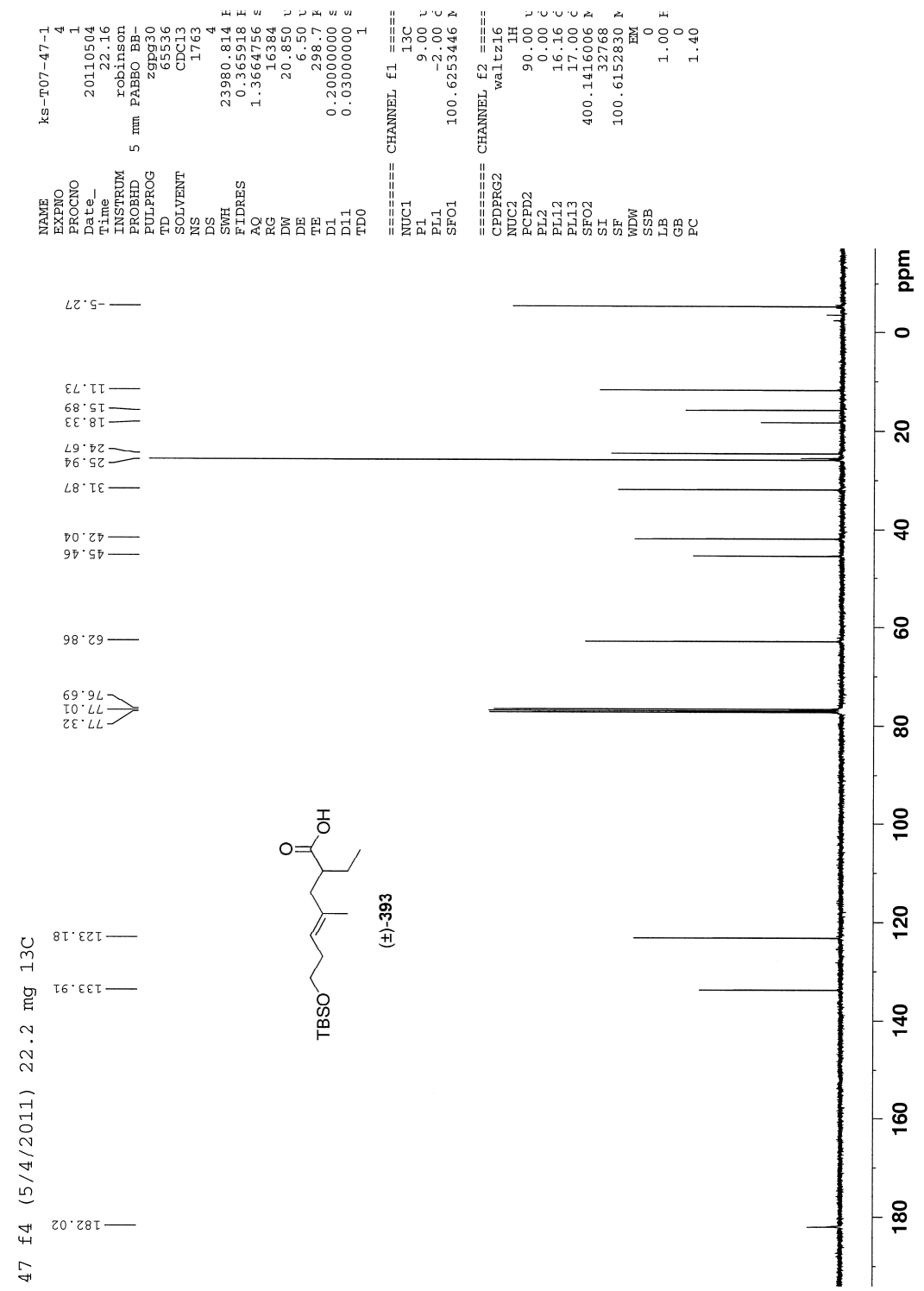

NAME ks-T07-45-1
EXPNO 2
PROCNO 1
Date_ 20110503
Time 13.25
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 71.8
DW 73.600 u
DE 6.50 u
TE 298.3 K
D1 2.00000000 s
TDO 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
45 f3 (5/3/2011)
7.282
5.326
5.311
5.307
5.292
4.968
4.967
4.894
4.891
4.888
3.656
3.639
3.623
2.327
2.308
2.290
1.899
1.884
1.880
1.869
1.864
1.855
1.852
1.850
1.838
1.745
1.707
1.688
1.670
1.651
0.989
0.971
0.952
0.908
0.054
TBSO
(±)-391
ppm
8
7
6
5
4
3
2
1
0
0.94
1.02
1.00
2.04
2.00
2.18
3.00
2.12
3.28
9.15
5.99

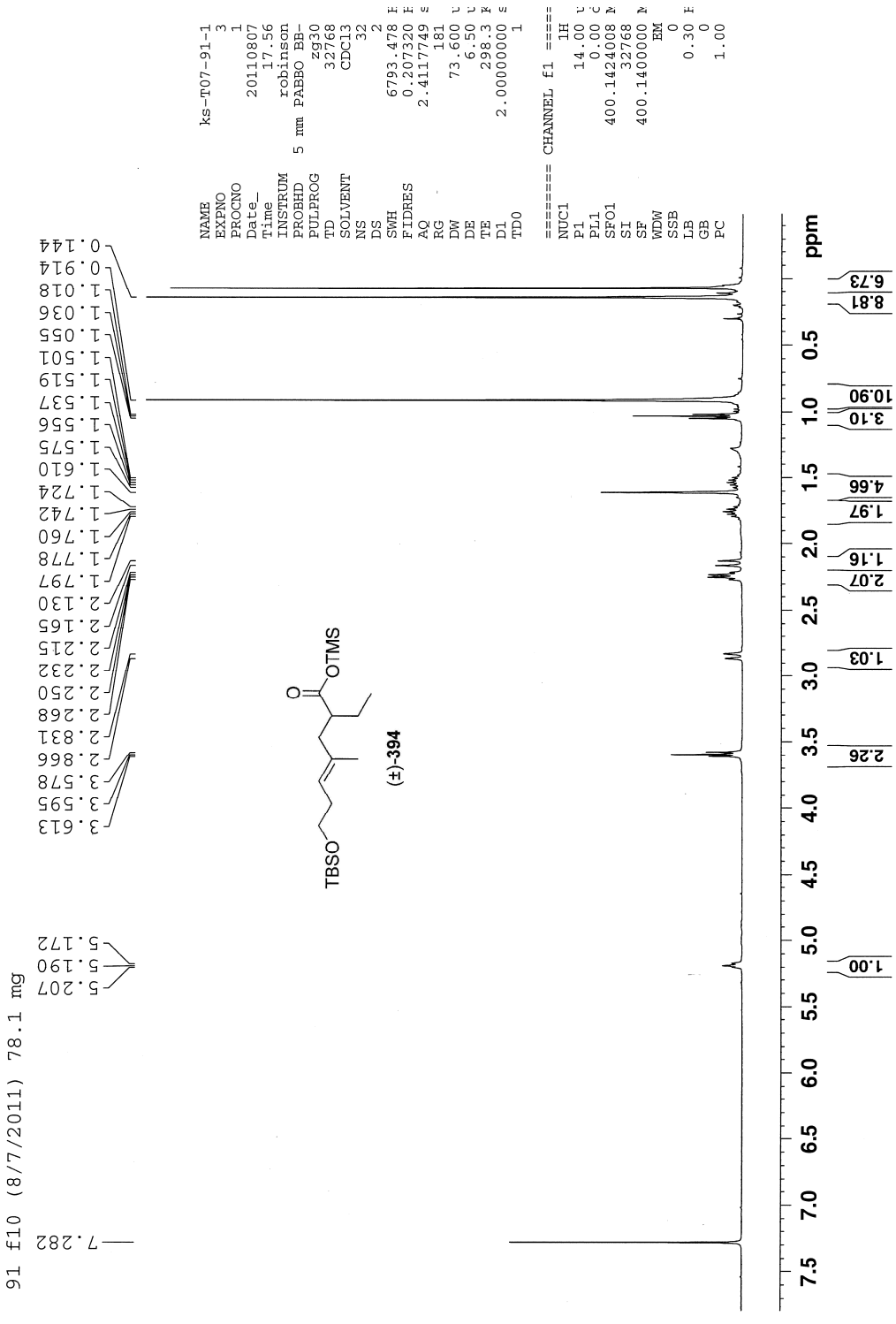
45 f3 (5/8/2011) 13C

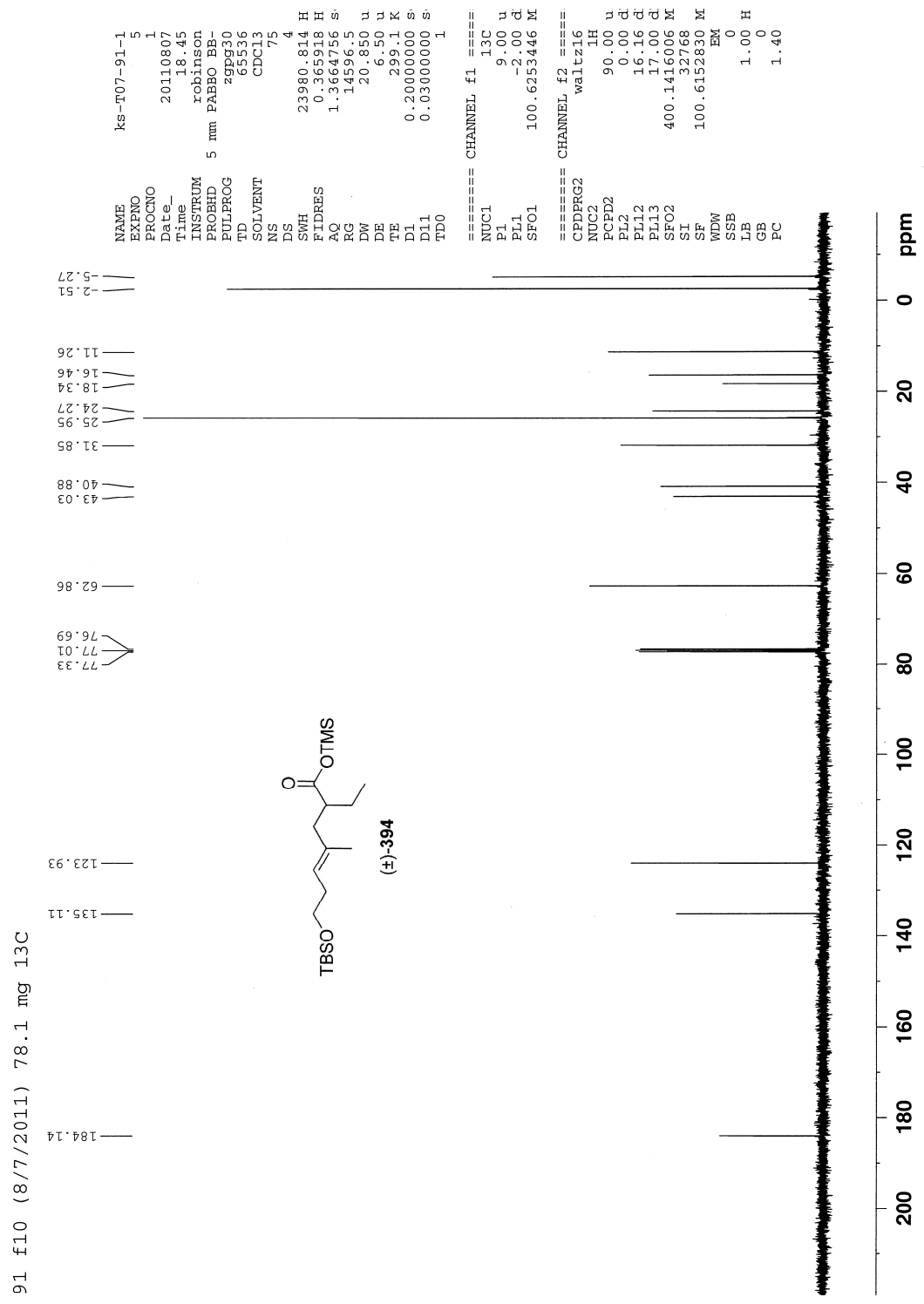


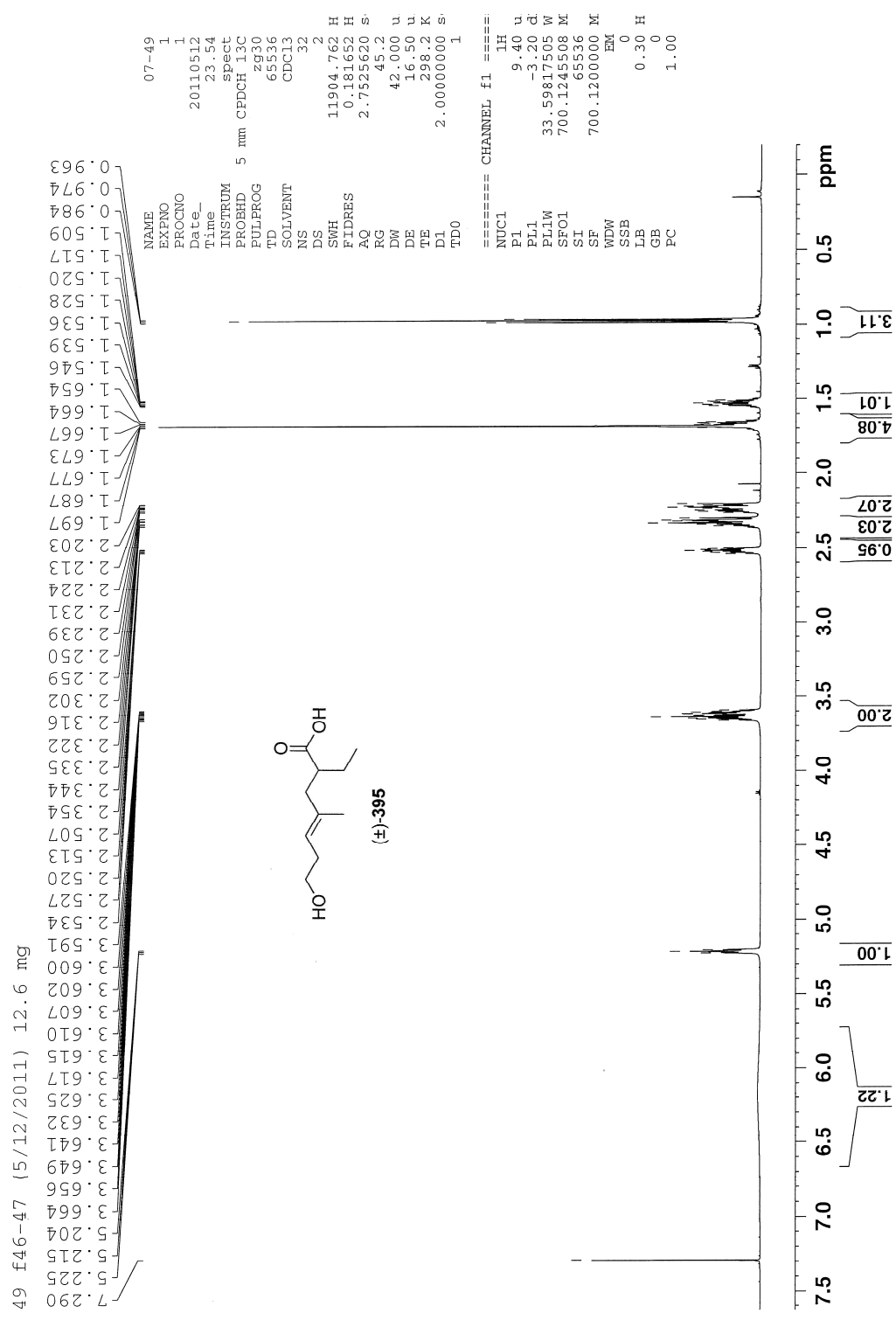
NAME	07-45
EXPNO	2
PROCNO	1
Date_	20110508
Time	16.47
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	100
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 use
DE	15.00 use
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

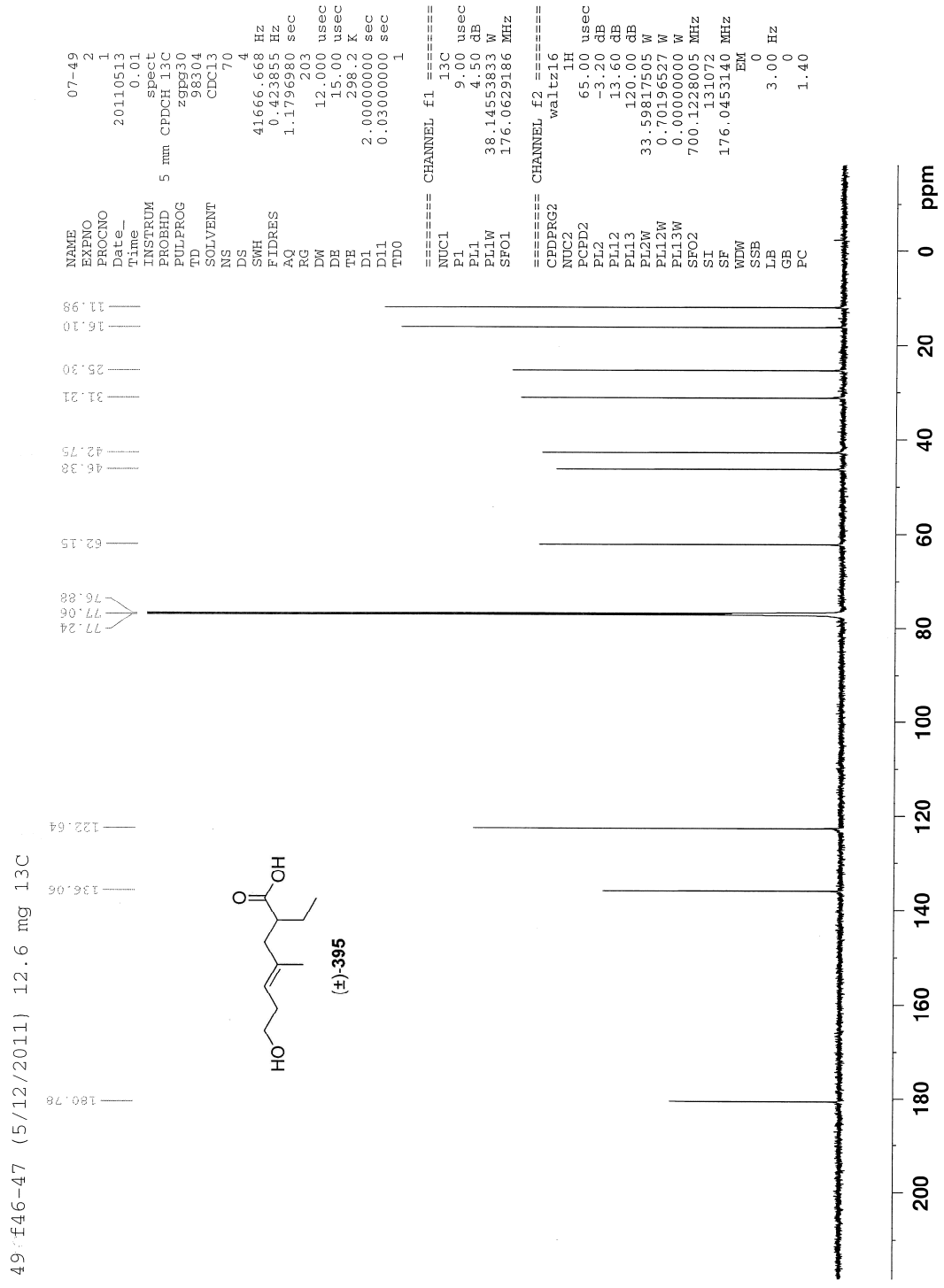

91 f46- (8/9/2011) 21.1 mg
(±)-393
TBSO
OH
O
NAME ks-T07-91-1
EXPNO 13
PROCNO 1
Date_ 20110809
Time 16.04
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 57
DW 73.600 u
DE 6.50 u
TE 298.2 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
7.282
5.319
5.223
5.207
5.205
5.189
5.187
3.603
3.598
3.585
3.567
2.510
2.505
2.491
2.486
2.471
2.452
2.381
2.361
2.347
2.328
2.268
2.250
2.233
2.215
2.186
2.168
2.152
2.134
1.655
1.641
1.625
1.623
1.607
1.586
1.581
1.567
1.562
1.549
ppm
1.00
2.05
1.14
1.20
2.05
1.04
3.19
2.17
13.59
6.23

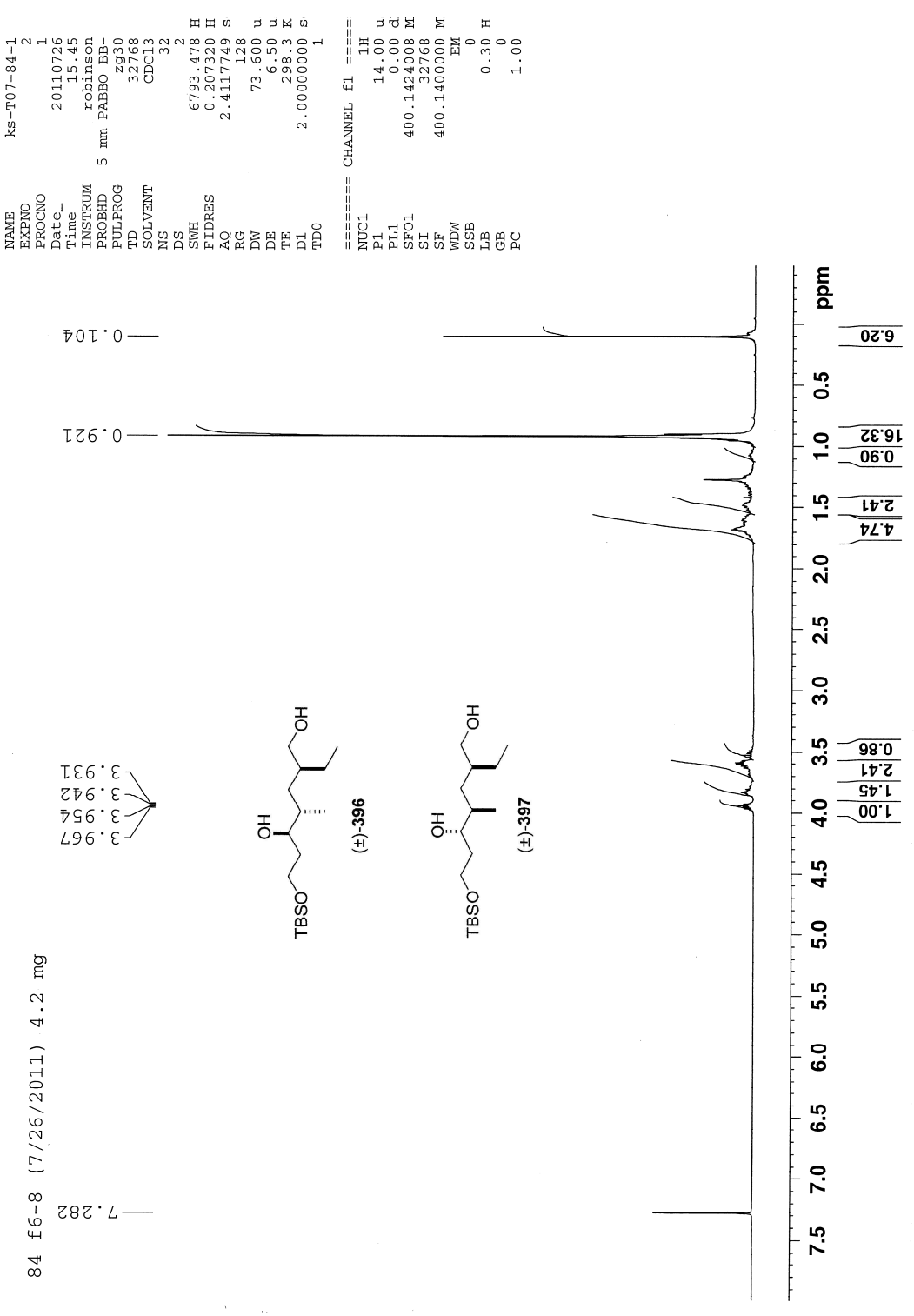

47 f4 (5/4/2011) 22.2 mg 13C
NAME ks-T07-47-1
EXPNO 4
PROCNO 1
Date_ 20110504
Time_ 22.16
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1763
DS 4
SWH 23980.814
FIDRES 0.365918
AQ 1.3664756
RG 16384
DW 20.850
DE 6.50
TE 298.7
D1 0.20000000
D11 0.03000000
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 9.00
PL1 -2.00
SFO1 100.6253446
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00
PL2 0.00
PL12 16.16
PL13 17.00
SFO2 400.1416006
SI 32768
SF 100.6152830
WDW EM
SSB 0
LB 1.00
GB 0
PC 1.40
-5.27
11.73
15.89
18.33
24.67
25.94
31.87
42.04
45.46
62.86
76.69
77.01
77.32
123.18
133.91
182.02
TBSO
OH
O
(±)-393
ppm
0
20
40
60
80
100
120
140
160
180


91 f10 (8/7/2011) 78.1 mg
7.282
5.207
5.190
5.172
3.613
3.595
3.578
2.866
2.831
2.268
2.250
2.232
2.215
2.165
2.130
1.797
1.778
1.760
1.742
1.724
1.610
1.575
1.556
1.537
1.519
1.501
1.055
1.036
1.018
0.914
0.144
TBSO
OTMS
O
(±)-394
NAME ks-T07-91-1
EXPNO 3
PROCNO 1
Date_ 20110807
Time 17.56
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478
FIDRES 0.207320
AQ 2.4117749
RG 181
DW 73.600
DE 6.50
TE 298.3
D1 2.00000000
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00
PL1 0.00
SFO1 400.1424008
SI 32768
SF 400.1400000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.00
2.26
1.03
2.07
1.16
1.97
4.66
3.10
10.90
8.81
6.73

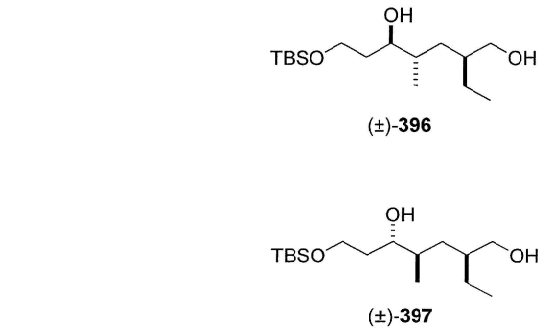

91 f10 (8/7/2011) 78.1 mg 13C
NAME ks-T07-91-1
EXPNO 5
PROCNO 1
Date_ 20110807
Time 18.45
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 75
DS 4
SWH 23980.814 H
FIDRES 0.365918 H
AQ 1.3664756 s
RG 14596.5
DW 20.850 u
DE 6.50 u
TE 299.1 K
D1 0.20000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
SFO1 100.6253446 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
SFO2 400.1416006 M
SI 32768
SF 100.6152830 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
-5.27
-2.51
11.26
16.46
18.34
24.27
25.95
31.85
40.88
43.03
62.86
76.69
77.01
77.33
123.93
135.11
184.14
TBSO
OTMS
O
(±)-394
200
180
160
140
120
100
80
60
40
20
0
ppm


49 f46-47 (5/12/2011) 12.6 mg
NAME 07-49
EXPNO 1
PROCNO 1
Date_ 20110512
Time 23.54
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 H
FIDRES 0.181652 H
AQ 2.7525620 s
RG 45.2
DW 42.000 u
DE 16.50 u
TE 298.2 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 9.40 u
PL1 -3.20 d
PL1W 33.59817505 W
SFO1 700.1245508 M
SI 65536
SF 700.1200000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
OH
O
HO
(±)-395
ppm
3.11
1.01
4.08
2.07
2.03
0.95
2.00
1.00
1.22


49:f46-47 (5/12/2011) 12.6 mg 13C
(±)-395
OH
O
HO
NAME 07-49
EXPNO 2
PROCNO 1
Date_ 20110513
Time 0.01
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDC13
NS 70
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
11.98
16.10
25.30
31.21
42.75
46.38
62.15
76.88
77.06
77.24
122.64
136.06
180.78
200
180
160
140
120
100
80
60
40
20
0
ppm


NAME ks-T07-84-1
EXPNO 2
PROCNO 1
Date_ 20110726
Time 15.45
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 128
DW 73.600 u
DE 6.50 u
TE 298.3 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
84 f6-8 (7/26/2011) 4.2 mg
7.282
0.921
0.104
3.967
3.954
3.942
3.931
TBSO
OH
(±)-396
TBSO
OH
(±)-397
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.00
1.45
2.41
0.86
4.74
2.41
0.90
16.32
6.20

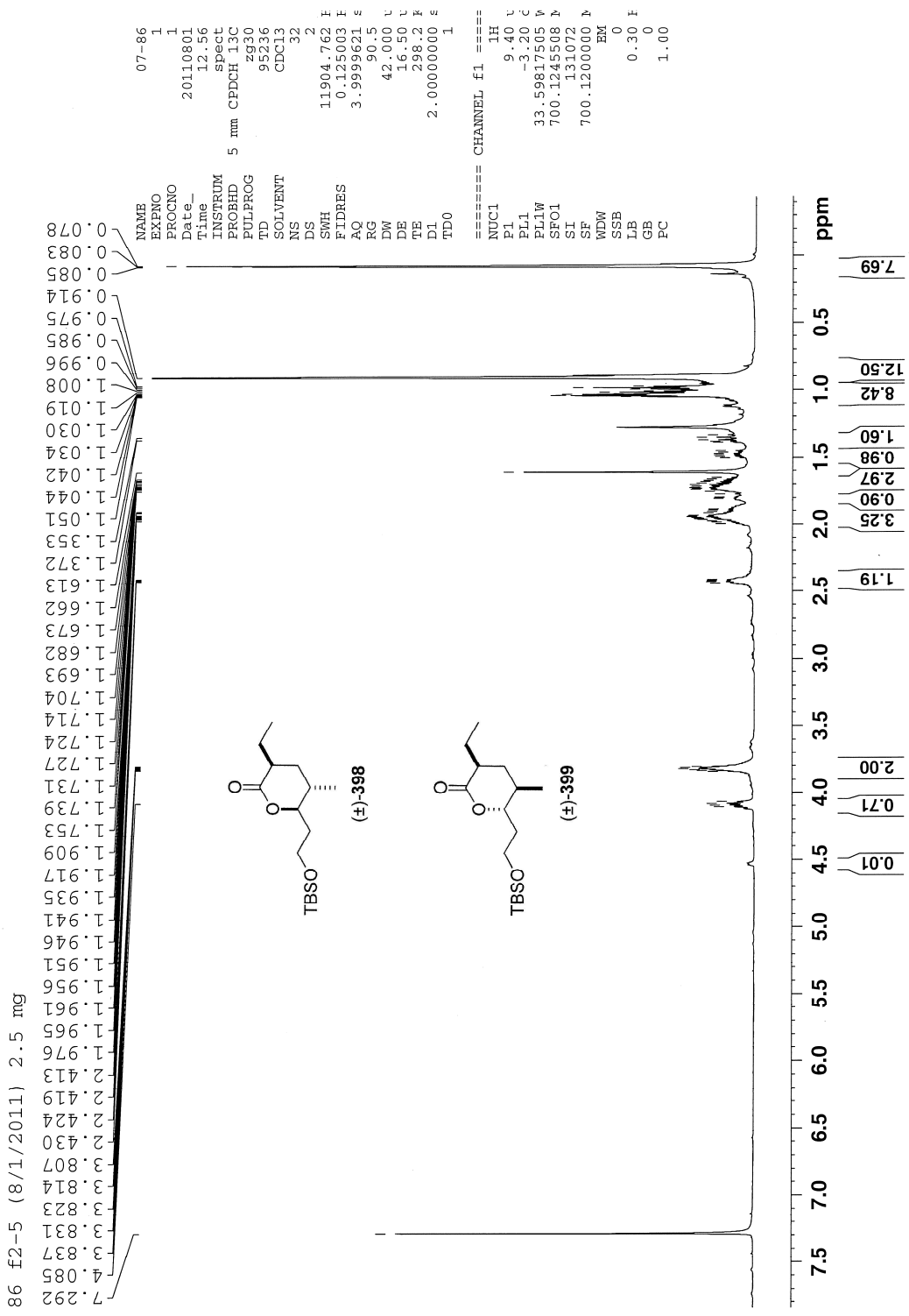
77 f5-10 (7/19/2011) 3.3 mg 13C

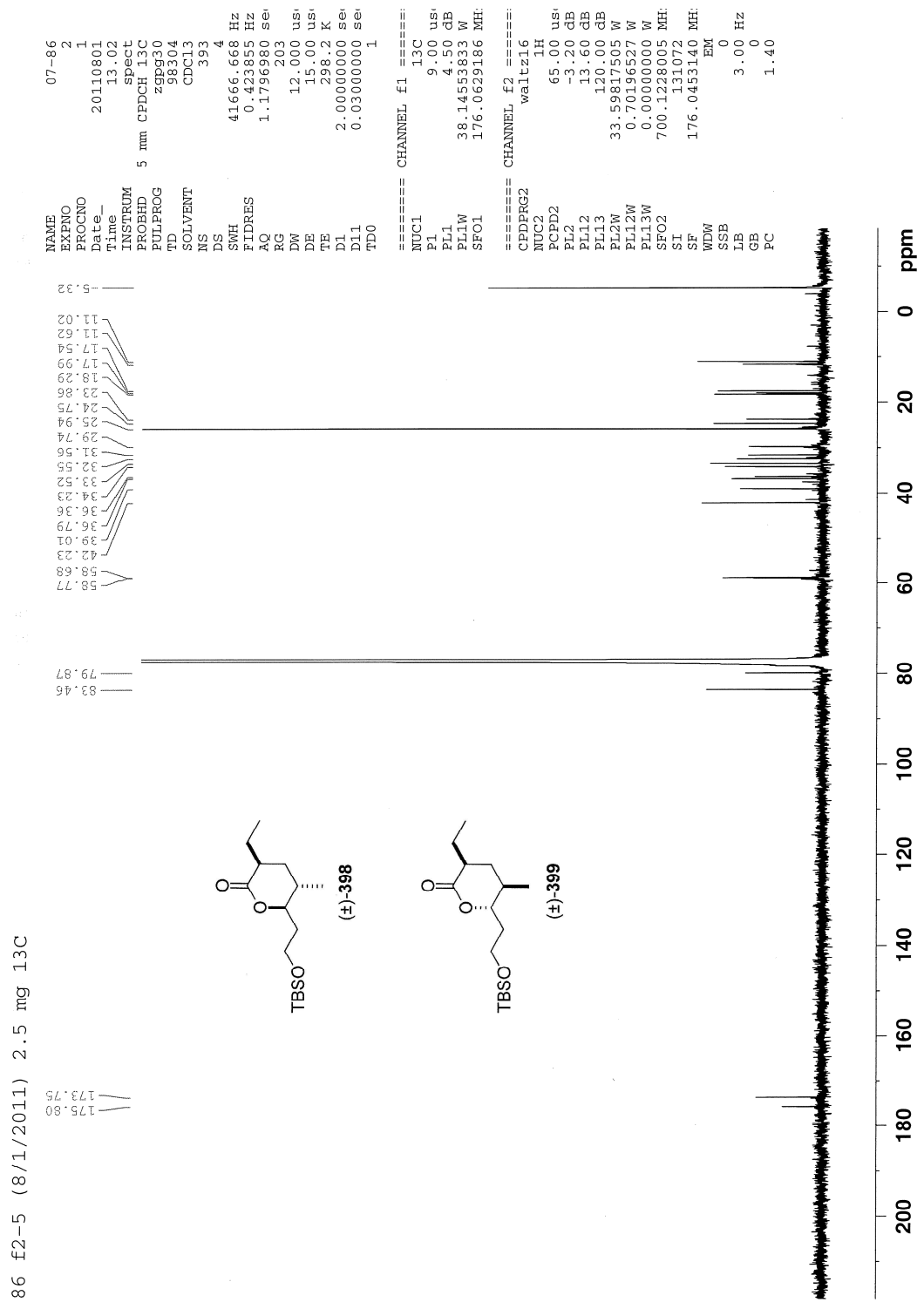


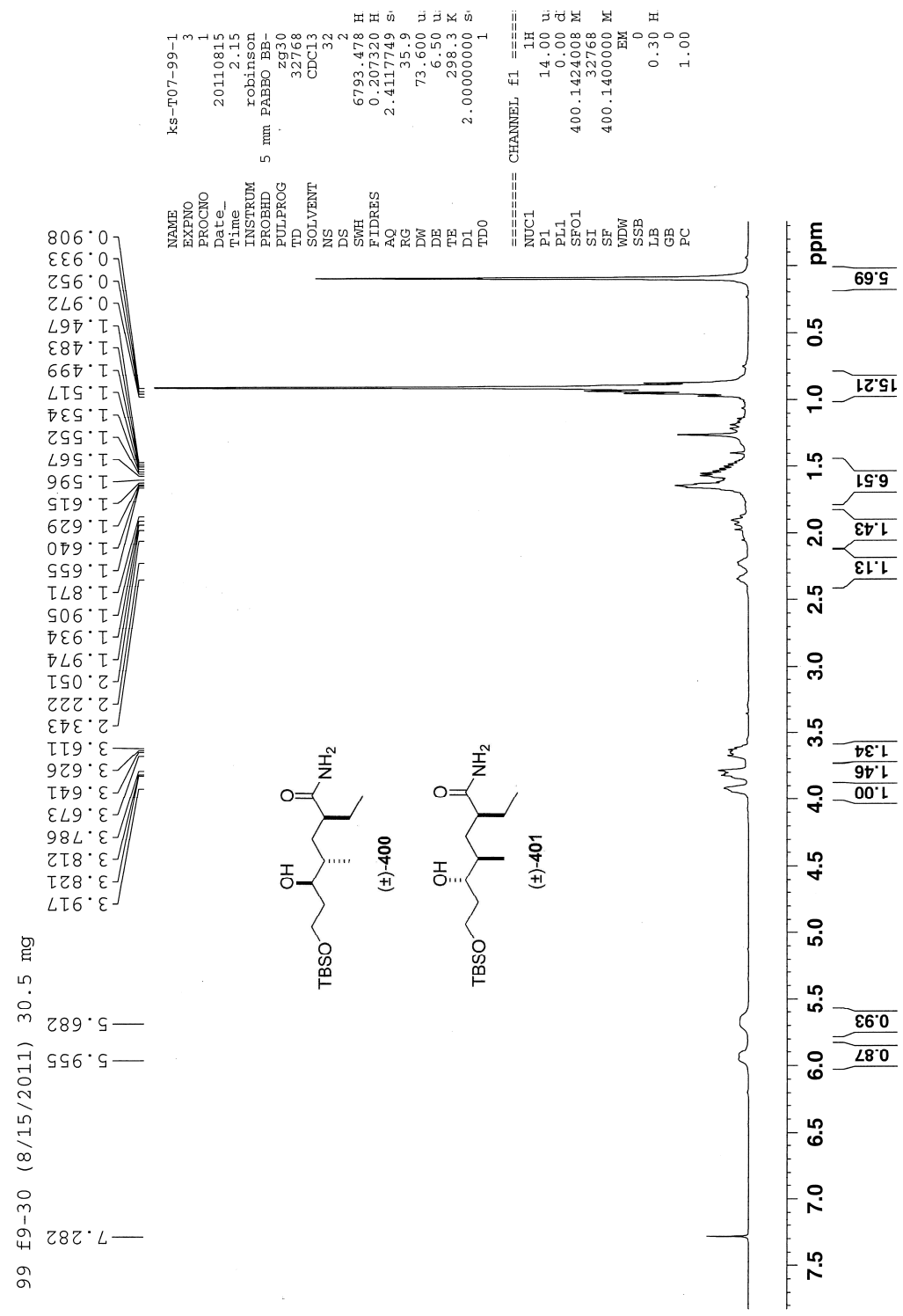
(±)-**396**

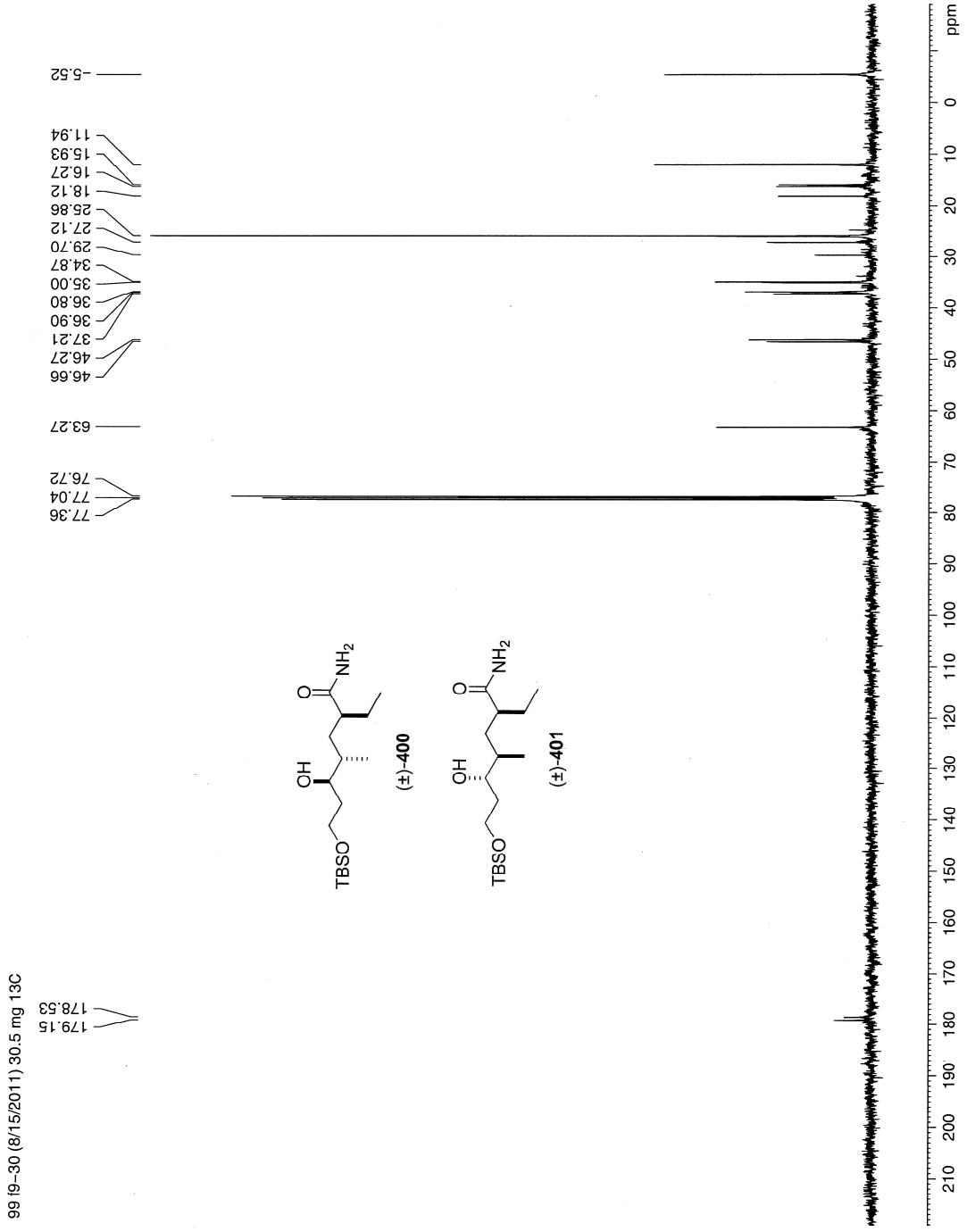
(±)-**397**

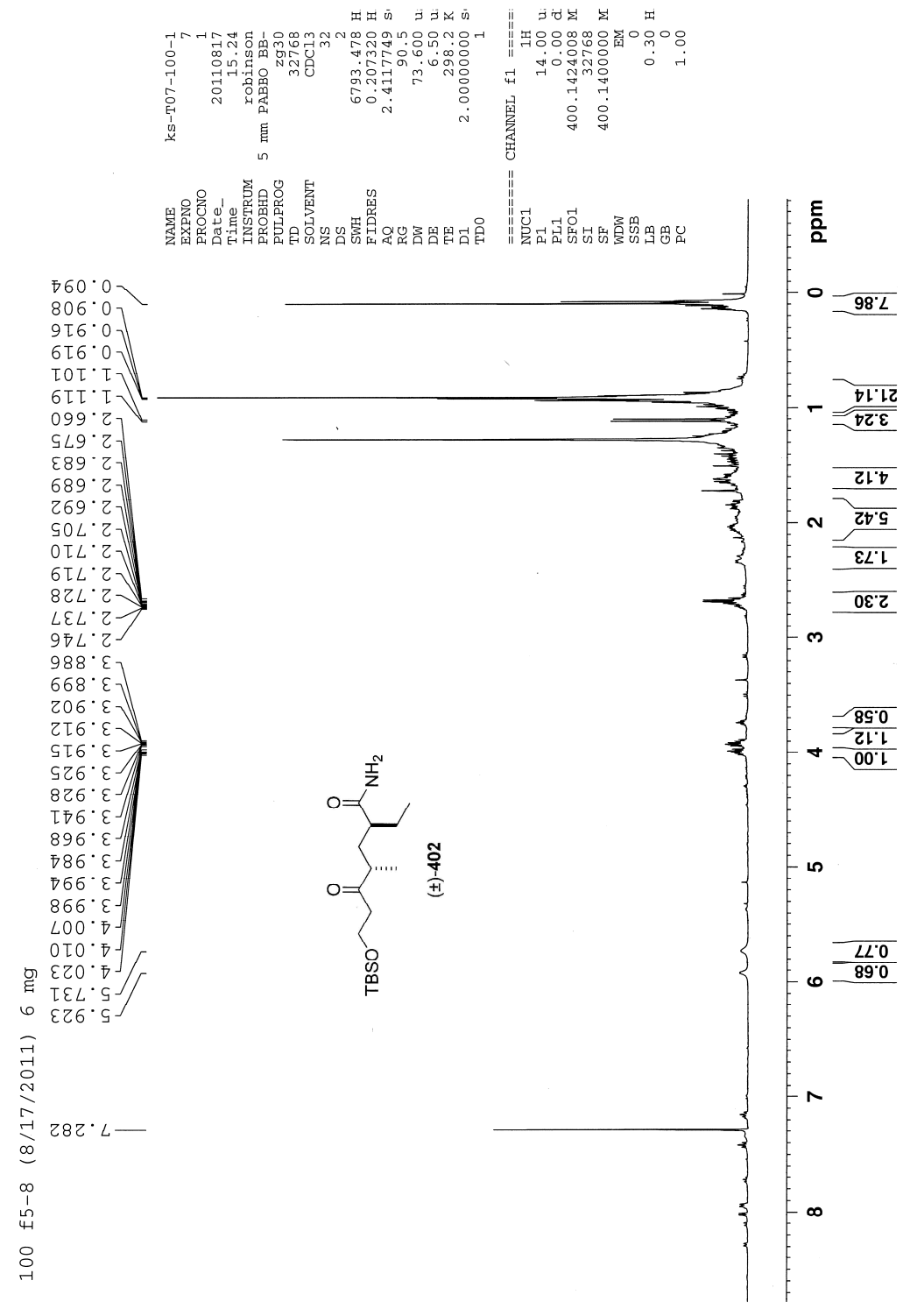
NAME	07-77
EXPNO	3
PROCNO	1
Date_	20110719
Time	16.05
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	592
DS	4
SWH	41666.668 H
FIDRES	0.423855 H
AQ	1.1796980 s
RG	203
DW	12.000 u
DE	15.00 u
TE	298.2 K
D1	2.00000000 s
D11	0.03000000 s
TD0	1
======== CHANNEL f1 =====	
NUC1	13C
P1	9.00 u
PL1	4.50 d
PL1W	38.14553833 W
SFO1	176.0629186 M
======== CHANNEL f2 =====	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 u
PL2	-3.20 d
PL12	13.60 d
PL13	120.00 d
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 M
SI	131072
SF	176.0453140 M
WDW	EM
SSB	0
LB	3.00 H
GB	0
PC	1.00

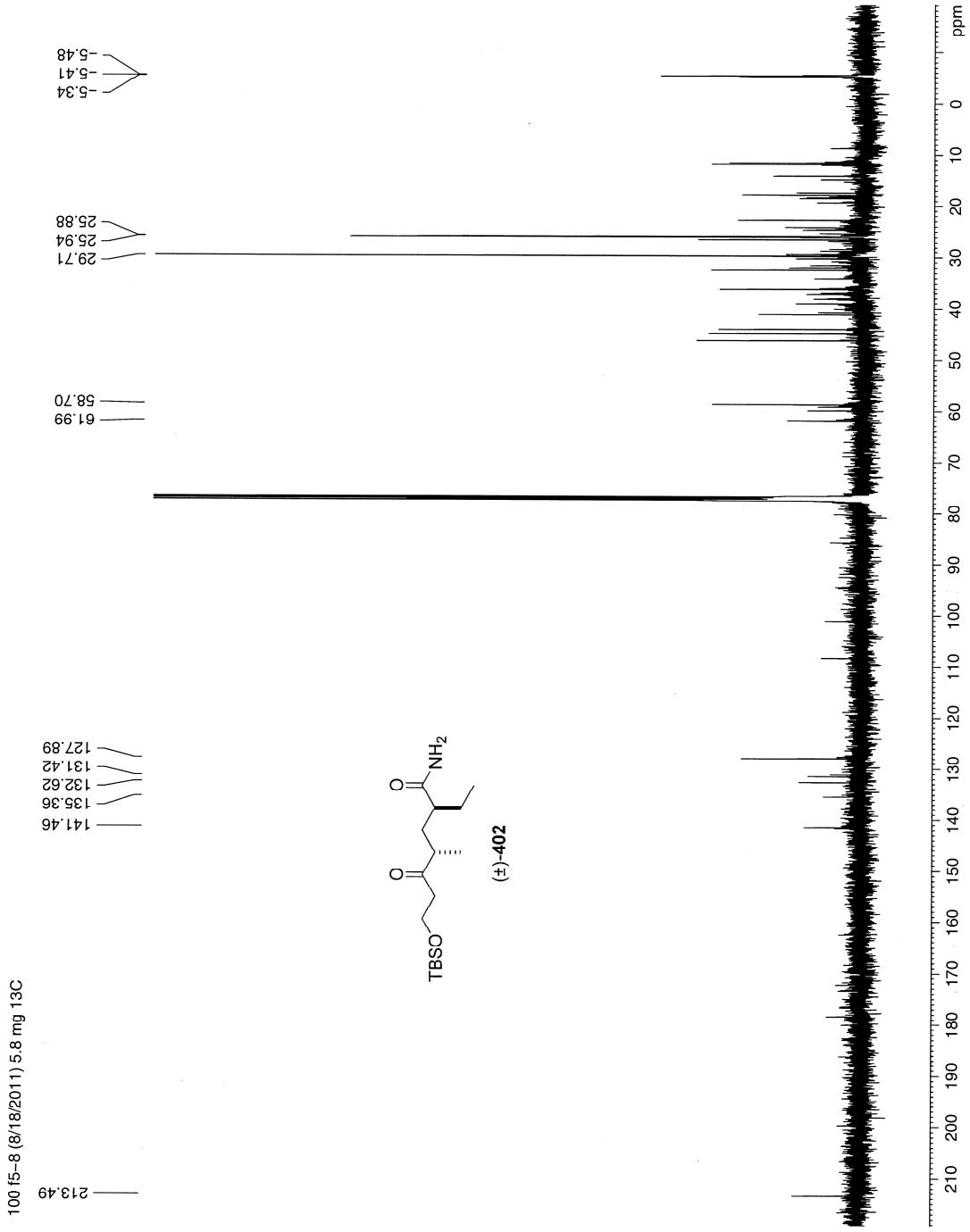

86 f2-5 (8/1/2011) 2.5 mg
NAME 07-86
EXPNO 1
PROCNO 1
Date_ 20110801
Time 12.56
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762
FIDRES 0.125003
AQ 3.9999621
RG 90.5
DW 42.000
DE 16.50
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 9.40
PL1 -3.20
PL1W 33.59817505
SFO1 700.1245508
SI 131072
SF 700.1200000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
TBSO
(±)-398
TBSO
(±)-399
ppm
7.69
12.50
8.42
1.60
0.98
2.97
0.90
3.25
1.19
2.00
0.71
0.01

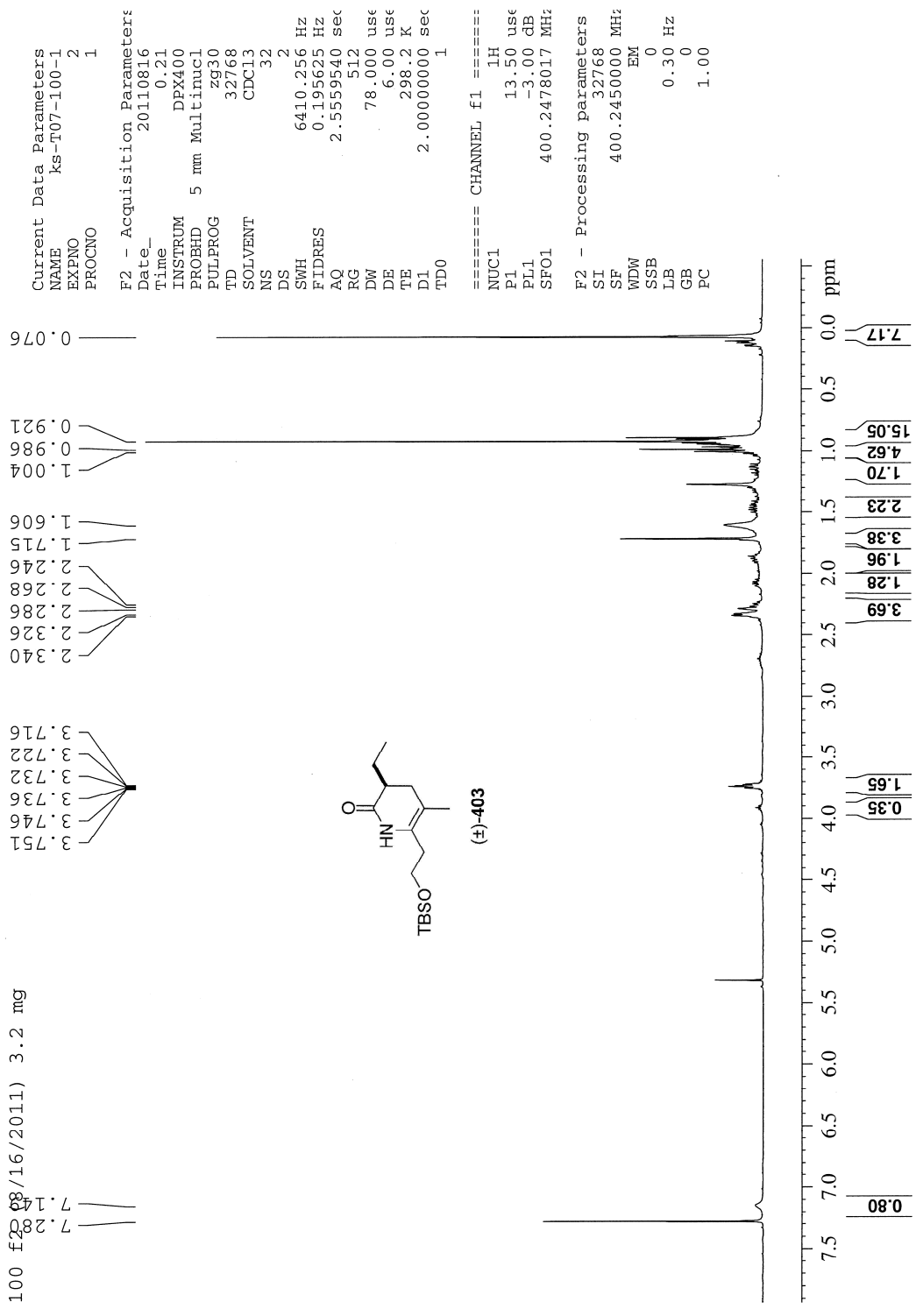

86 f2-5 (8/1/2011) 2.5 mg 13C
NAME 07-86
EXPNO 2
PROCNO 1
Date_ 20110801
Time 13.02
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 393
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 se
RG 203
DW 12.000 us
DE 15.00 us
TE 298.2 K
D1 2.00000000 se
D11 0.03000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 9.00 us
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 us
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MH
SI 131072
SF 176.0453140 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
175.80
173.75
83.46
79.87
58.77
58.68
42.23
39.01
36.79
36.36
34.23
33.52
32.55
31.56
29.74
25.94
24.75
23.86
18.29
17.99
17.54
11.62
11.02
-5.32
TBSO
(±)-398
TBSO
(±)-399
200
180
160
140
120
100
80
60
40
20
0
ppm

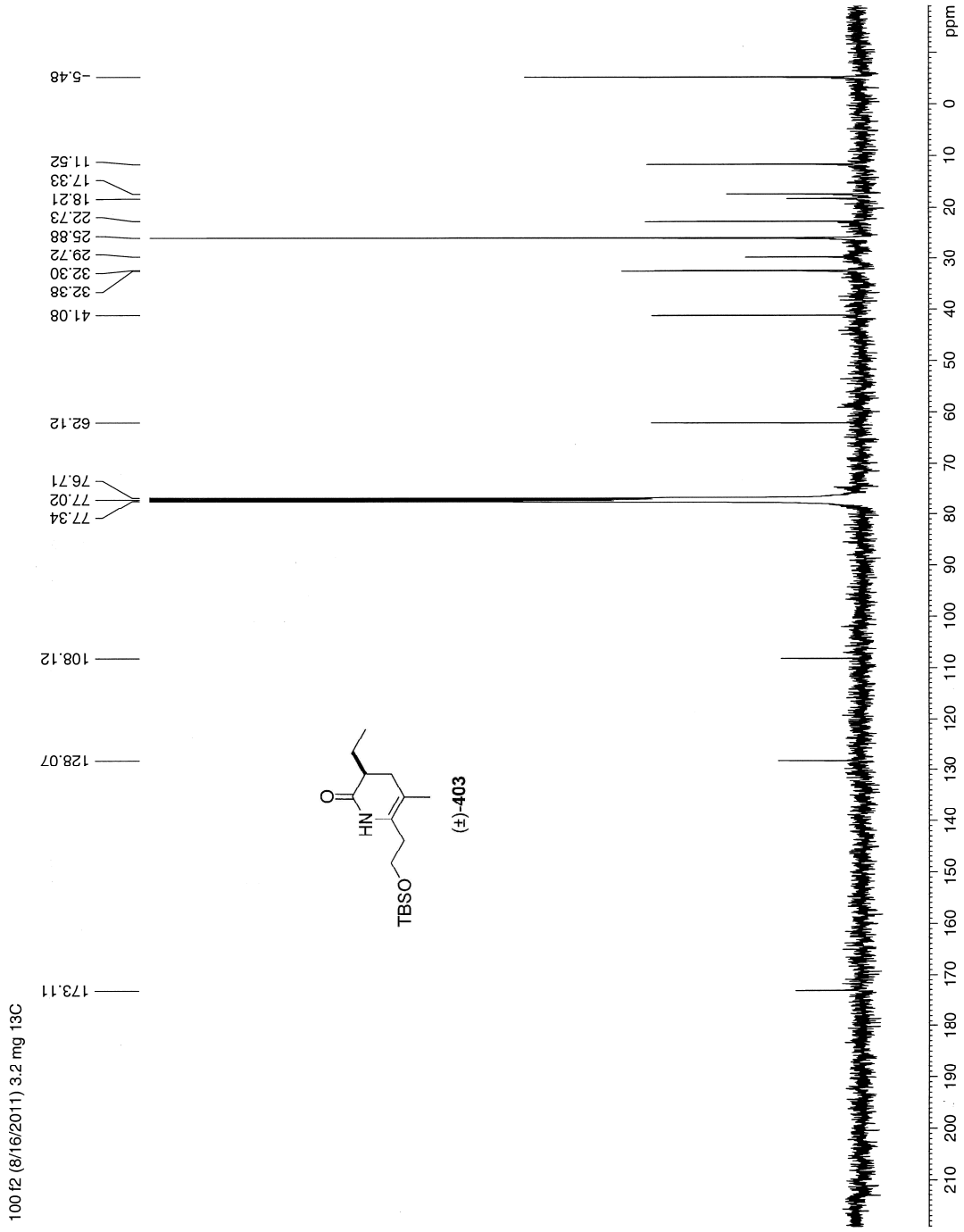

99 f9-30 (8/15/2011) 30.5 mg
NAME ks-T07-99-1
EXPNO 3
PROCNO 1
Date_ 20110815
Time 2.15
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 35.9
DW 73.600 u
DE 6.50 u
TE 298.3 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
PL1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
7.282
5.955
5.682
3.917
3.821
3.812
3.786
3.673
3.641
3.626
3.611
2.343
2.222
2.051
1.974
1.934
1.905
1.871
1.655
1.640
1.629
1.615
1.596
1.567
1.552
1.534
1.517
1.499
1.483
1.467
0.972
0.952
0.933
0.908
TBSO
OH
O
NH2
(±)-400
(±)-401
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
5.69
15.21
6.51
1.43
1.13
1.34
1.46
1.00
0.93
0.87

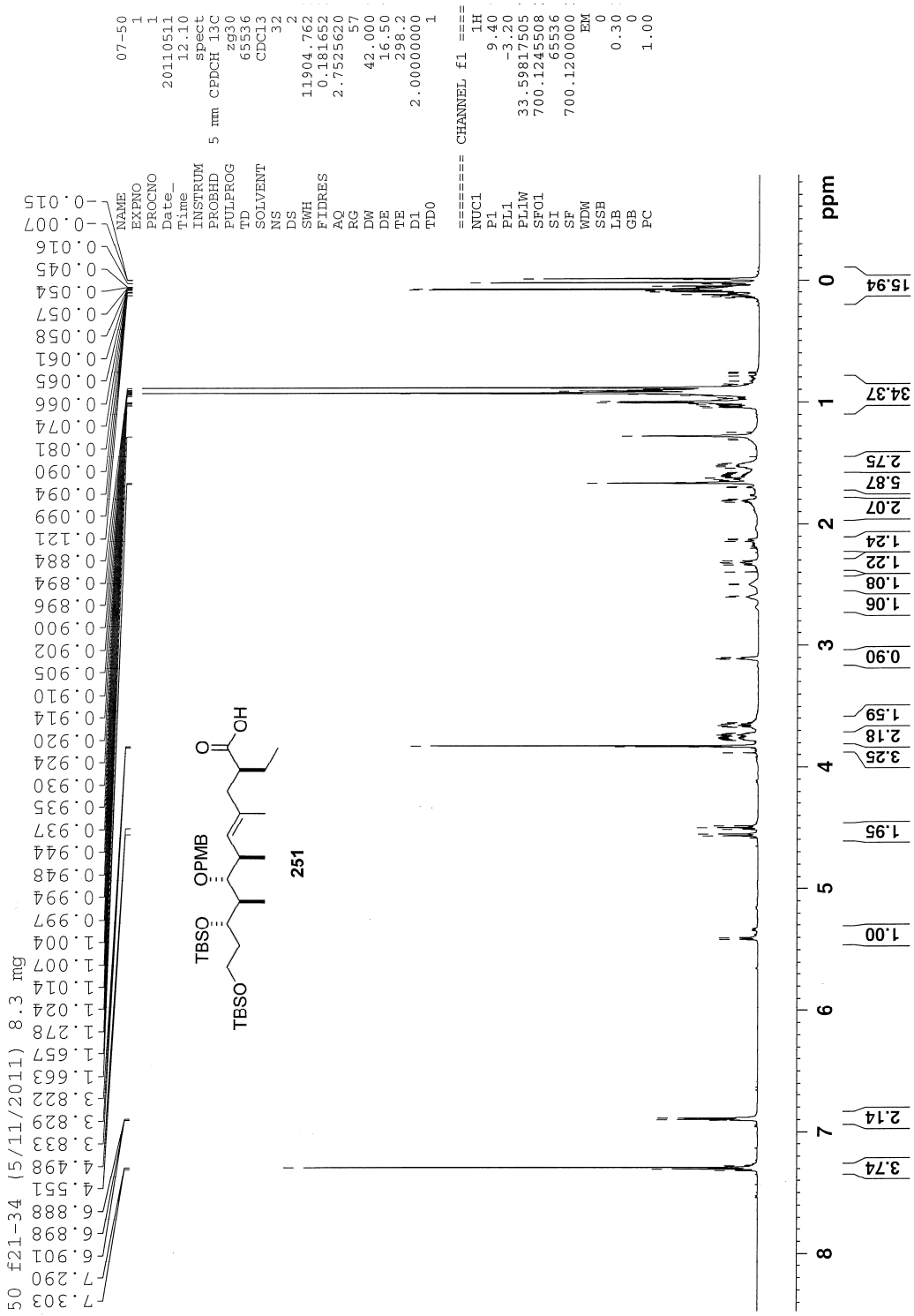

99 f9--30 (8/15/2011) 30.5 mg 13C
179.15
178.53
77.36
77.04
76.72
63.27
46.66
46.27
37.21
36.90
36.80
35.00
34.87
29.70
27.12
25.86
18.12
16.27
15.93
11.94
-5.52
ppm
TBSO
OH
NH2
O
(±)-400
(±)-401

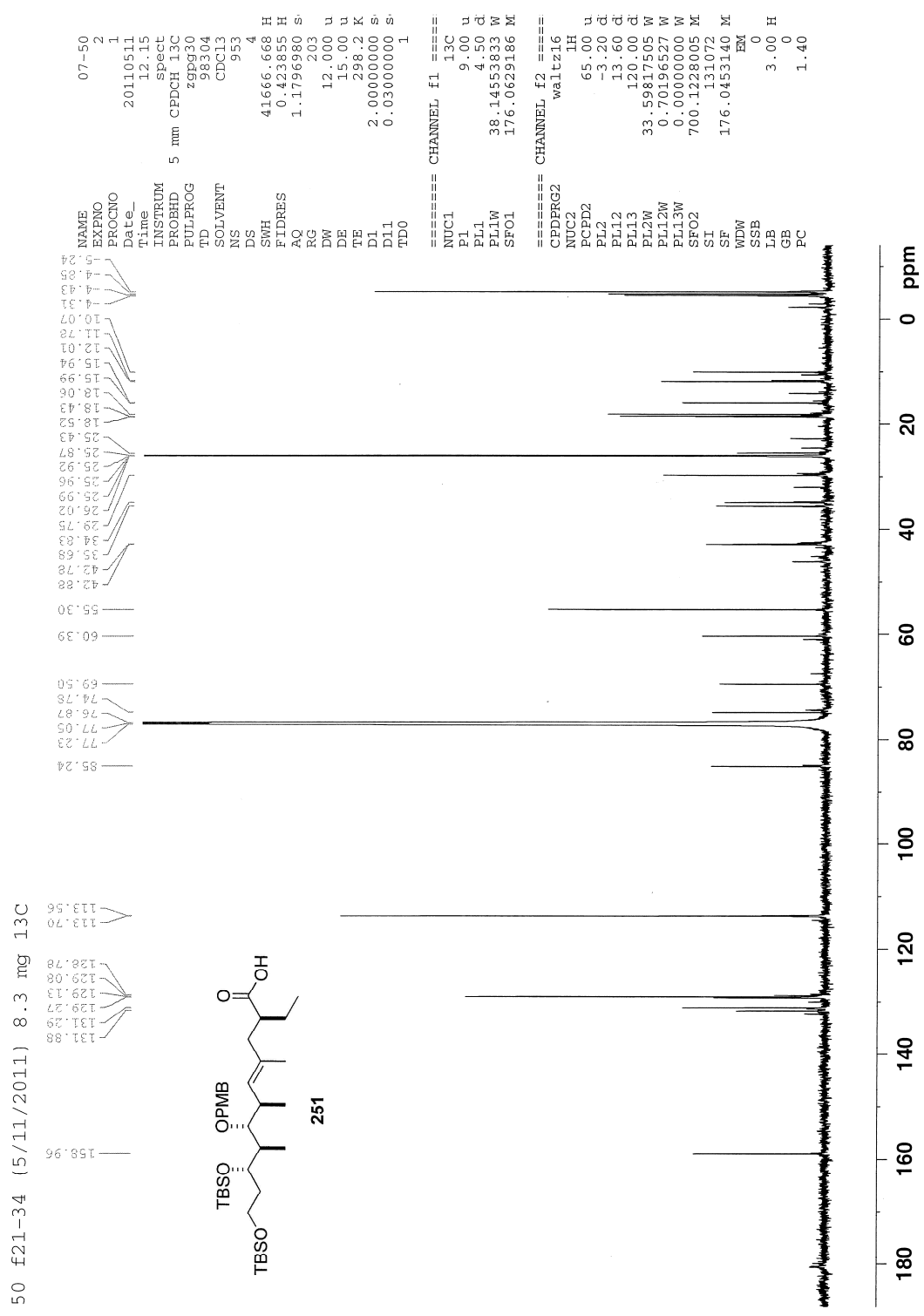

100 f5-8 (8/17/2011) 6 mg
NAME ks-T07-100-1
EXPNO 7
PROCNO 1
Date_ 20110817
Time 15.24
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 90.5
DW 73.600 u
DE 6.50 u
TE 298.2 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.00
TBSO
NH2
(±)-402
ppm
7.86
3.24
21.14
4.12
5.42
1.73
2.30
1.00
1.12
0.58
0.68
0.77

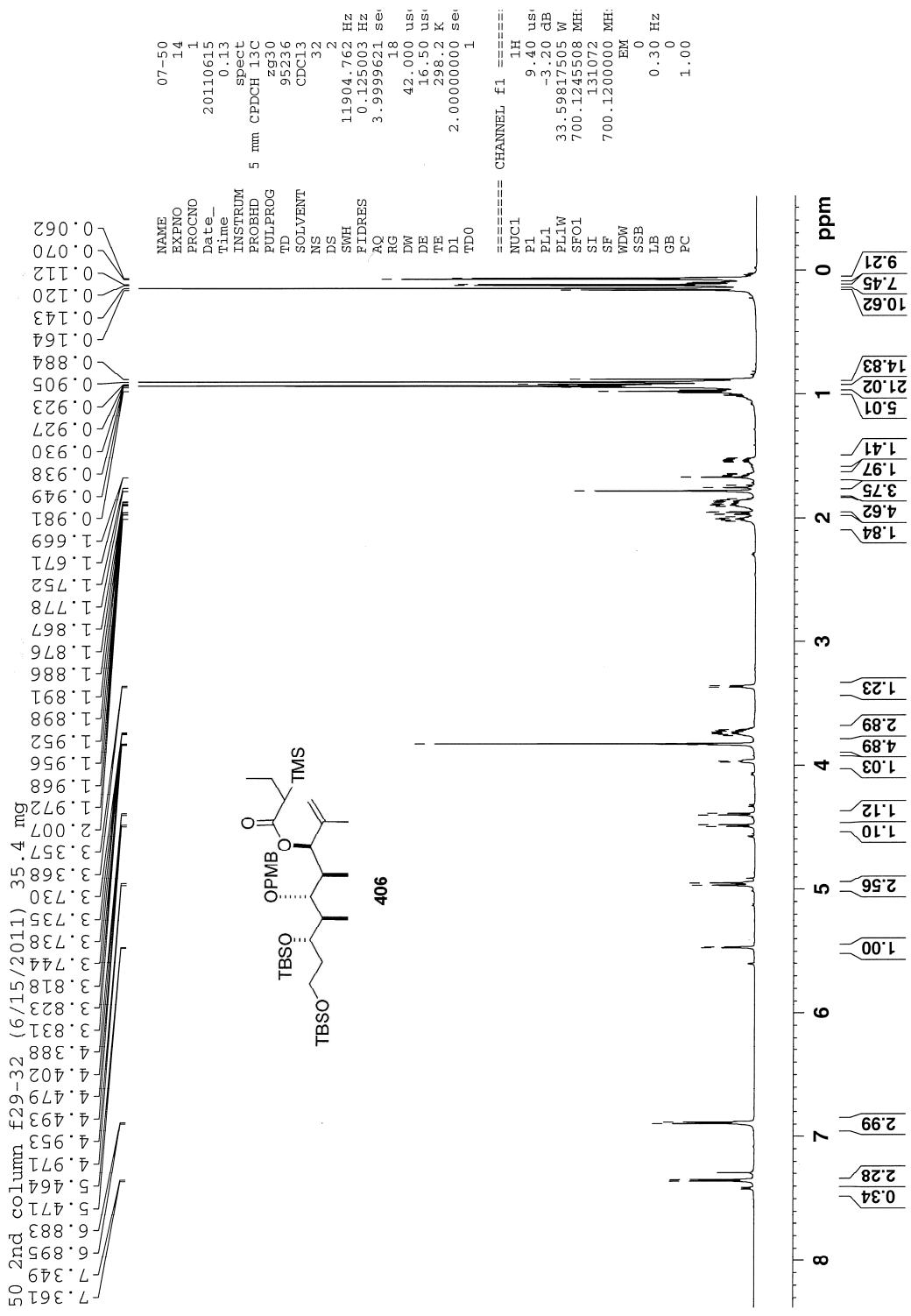

100 f5–8 (8/18/2011) 5.8 mg 13C
213.49
141.46
135.36
132.62
131.42
127.89
61.99
58.70
29.71
25.94
25.88
-5.34
-5.41
-5.48
TBSO
O
O
NH2
(±)-402
ppm

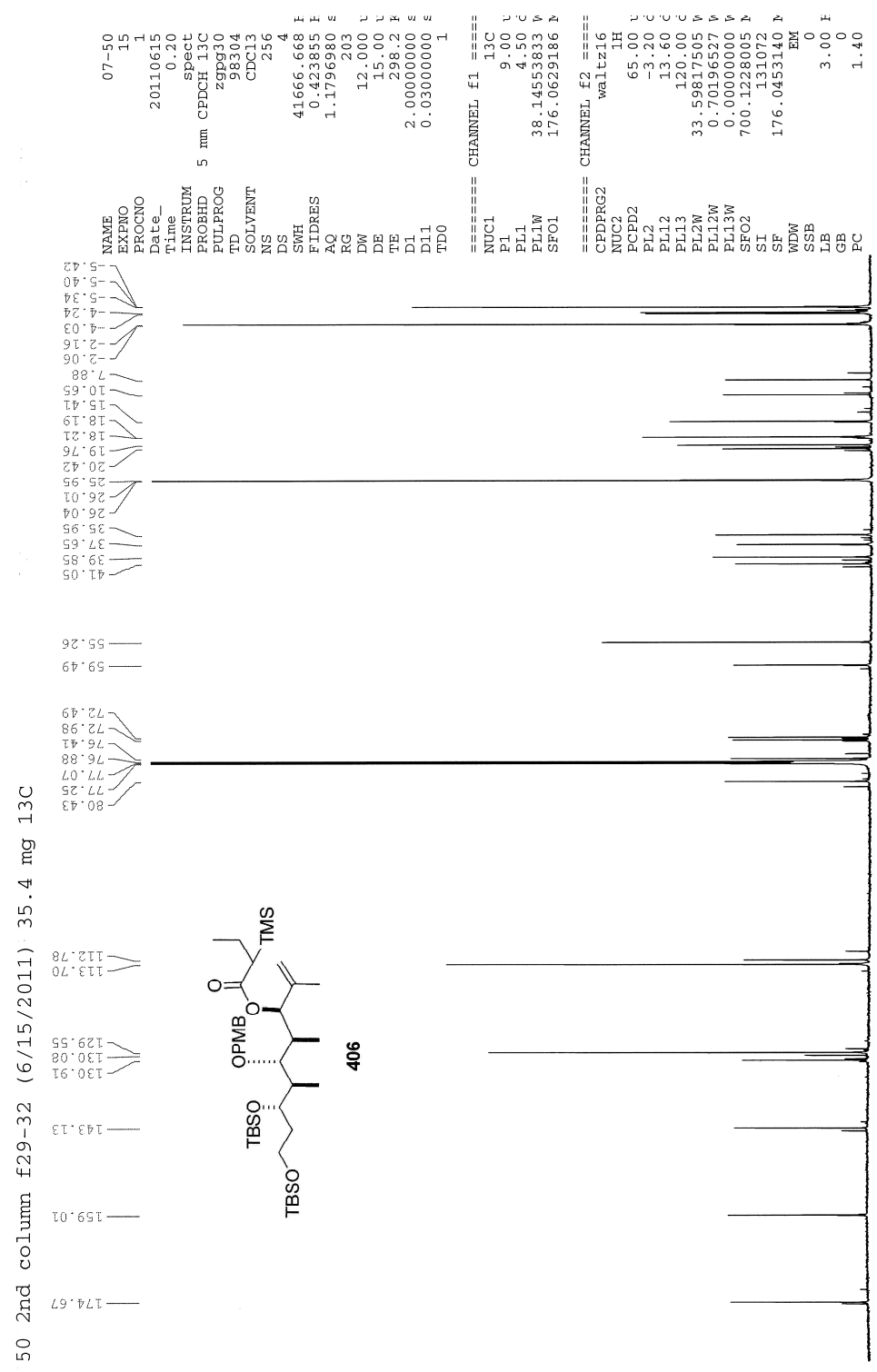

Current Data Parameters
NAME ks-T07-100-1
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110816
Time 0.21
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 use
DE 6.00 use
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 use
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
100 f2 08/16/2011) 3.2 mg
0.076
0.921
0.986
1.004
1.606
1.715
2.246
2.268
2.286
2.326
2.340
3.716
3.722
3.732
3.736
3.746
3.751
7.143
7.287
HN
O
TBSO
(±)-403
0.80
1.65
0.35
3.69
1.28
1.96
3.38
2.23
1.70
4.62
15.05
7.17
ppm


100 f2 (8/16/2011) 3.2 mg 13C
-5.48
11.52
17.33
18.21
22.73
25.88
29.72
32.30
32.38
41.08
62.12
76.71
77.02
77.34
108.12
128.07
173.11
TBSO
HN
O
(±)-403
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210


50 f21-34 (5/11/2011) 8.3 mg
NAME 07-50
EXPNO 1
PROCNO 1
Date_ 20110511
Time 12.10
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762
FIDRES 0.181652
AQ 2.752562
RG 57
DW 42.000
DE 16.50
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 9.40
PL1 -3.20
PL1W 33.59817505
SFO1 700.1245508
SI 65536
SF 700.1200000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
TBSO
OPMB
TBSO
O
OH
251
ppm
15.94
34.37
2.75
5.87
2.07
1.24
1.22
1.08
1.06
0.90
1.59
2.18
3.25
1.95
1.00
2.14
3.74


50 f21-34 (5/11/2011) 8.3 mg 13C
NAME 07-50
EXPNO 2
PROCNO 1
Date_ 20110511
Time 12.15
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 953
DS 4
SWH 41666.668 H
FIDRES 0.423855 H
AQ 1.1796980 s
RG 203
DW 12.000 u
DE 15.00 u
TE 298.2 K
D1 2.00000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 4.50 d
PL1W 38.14553833 W
SFO1 176.0629186 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 u
PL2 -3.20 d
PL12 13.60 d
PL13 120.00 d
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 M
SI 131072
SF 176.0453140 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
-5.24
-4.85
-4.43
-4.31
10.07
11.72
12.01
15.94
15.99
18.06
18.43
18.52
25.43
25.87
25.92
25.96
25.99
26.02
29.75
34.03
35.68
42.78
42.88
55.30
60.39
69.50
74.78
76.87
77.05
77.23
85.24
113.56
113.70
128.78
129.08
129.13
129.27
131.29
131.88
158.96
TBSO
OPMB
TBSO
O
OH
251
0
20
40
60
80
100
120
140
160
180
ppm


50 2nd column f29-32 (6/15/2011) 35.4 mg
NAME 07-50
EXPNO 14
PROCNO 1
Date_ 20110615
Time 0.13
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 se
RG 18
DW 42.000 us
DE 16.50 us
TE 298.2 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 9.40 us
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MH
SI 131072
SF 700.1200000 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TMS
O
OPMB
TBSO
TBSO
406
ppm


50 2nd column f29-32 (6/15/2011) 35.4 mg 13C
406
TBSO
OPMB
TBSO
TMS
O
O
ppm